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## The Edward Stirling Lectures.

### LECTURE II: SOME FUNDAMENTALS IN INFLAMMATION.

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God offers to every mind the choice between truth and repose. Take which you please—you can never have both.—RALPH WALDO EMERSON: "Essays."

It was Clifford Allbutt who said that he always advised students who asked him to suggest a subject for a thesis for their examinations to investigate one of the commonest and best-understood conditions; they would find that there were many hiatuses in our knowledge of it to provide ample opportunities for fresh study. Tonight we are to consider the commonest phenomenon in pathology.

Inflammation occurs in many forms and has many exciting causes, so for convenience it is proposed to deal principally with the more rapidly developing (that is, acute) forms and with those which follow bacterial invasion.

#### Definition.

One of the major causes of uncertainty in understanding many natural processes is the lack of satisfactory definitions or the confusion surrounding definitions. For this reason it is worth while spending a little time considering the problem of definition.

The first difficulty is psychical—almost universally it is demanded that a definition be complete but also brief and concise. When one appreciates that in so precise a science as mathematics brevity may be misleading, it is more easily understood that in the biological sciences conciseness may not be practicable.

The very nature of many groups of closely related pathological conditions, with their poorly defined boundaries, provides a dilemma not easily resolved. It is well shown in that heterogeneous horde, the neoplasms. In the case of inflammatory conditions we have just as many varieties, and if we would reduce them to some sort of order numerous variables must be considered. Any brief statement in general terms, therefore, is likely to offend those who have a sublime faith in the sharp demarcation between different conditions and a clear-cut perimeter for all. It is necessary to remember that no brief definition of life, growth or similar broad concept is adequate, and that the changes in inflammation are bound up with these. Thus any definition is certain neither to include all conditions which could be regarded as coming within its scope nor to exclude others which do not.

A further embarrassment arises from our mode of use of words. This may be from careless usage, because words often have more than one meaning, or because meanings of words change. All these things have happened with the term inflammation, giving the obvious consequent confusion.

The large number of definitions extant, even though most possess common features, indicates that the fundamental nature of the processes is not always clear. The most commonly accepted version is that "inflammation is the reaction of tissues to injury". The trouble is that the word "reaction" immediately takes on vital attributes. I know that arguments, often vehement and usually plausible, are raised against such a statement; but they savour of casuistry. Of course, the use of the term as it is applied in physics and chemistry is unassailable; but the very fact that the question of its meaning arises as an apparently inevitable perennial shows that this usage is not the common one in pathology.

Even more unsatisfactory, except that there is no subterfuge about it, is the inclusion of a blatantly purposive ingredient in the definition.<sup>1</sup> This teleological point of view is one that has always been a source of polemics and deserves some discussion. Before temporarily leaving the

<sup>1</sup> Delivered on May 25 and 27, 1948, at Adelaide.

subject of definition, I would suggest that the only safe one is that "inflammation is the series of changes which follows an injury to living tissues". We shall return to this.

#### *Teleology in Inflammation.*

An intense interest in the causes of phenomena is natural and inevitable. It is also natural that we should like to imagine that we have an understanding of the final cause or, as we usually regard it, the purpose behind phenomena. When we go back to Aristotle we find that he took into consideration various causes—material, formal, efficient and final kinds—of which the final cause or purpose was only relatively unimportant. In the second century A.D. Galen developed a philosophical system depending on humours. Everything was explained in terms of humours as final causes—and progress ceased for over a thousand years. It has been said that it is not reasonable to blame Galen for the progress that did not occur in this period. Nevertheless, he did supply a philosophical *placebo* which was eagerly accepted by his followers in lieu of actual observations. It is noteworthy that his observations (of a very high order) were forgotten or disregarded in favour of dogma—a characteristic of human nature.

This has been the invariable history of the teleological point of view. Naturally, if the final cause of any condition is understood, what further investigation is necessary? But time and further study have always shown that, though thoroughly satisfying at the time, the teleological view is but a mirage.

It is instructive to consider that our ideas of purpose cannot be other than alternative and roundabout ways of stating what we know of a phenomenon. We observe that saliva moistens our food; but many of us prefer to say that the purpose of salivary secretion is to provide moisture for our food. When the blood pressure falls suddenly, fainting and adoption of the horizontal position are said to have as their purpose the restoration of the cerebral circulation. Examples could be elaborated *ad infinitum*.

When we consider the history of our knowledge of inflammation, this point is well demonstrated. During the witchcraft period an area of inflammation and an abscess obviously had as its purpose the escape of evil spirits from the body. At a later period when the idea of humours was favoured, this inflammation was obviously the means by which various humours were localized and also allowed to escape. At another period it was black bile.

When histological study showed the cellular character of the process, then clearly the wandering cells had as their purpose the localization of the bacterial infection. We can all remember the time when even the discovery of organisms outside a leucocyte "barrier" still did not significantly influence the ideas about it. At present the purposive idea revolves around antibodies. The important point is that each of these ideas, determined by current hypotheses, achieved nothing but to give a false air of profundity to incomplete or misleading statements of the processes concerned.

Every investigator who collects new observations and opens up new fields is, in the very accumulation of these observations and the necessary associated hypotheses, erecting a barrier to further progress. It seems inevitable that progress should occur only in small steps. However, progress is possible because fortunately individuals arise to carry on the flame with a fresh vigour. It is essential that we should be thoroughly aware of these inherent limitations and appreciate that the most important part of them is the assumption that we are achieving something by imagining that we know anything of final causes. Teleology is a sedative, and as was suggested earlier, its acceptance is incompatible with truth. Any question of teleological and purposive approach therefore must be excluded rigidly from our ideas if we are to progress.

To return, therefore, for a moment to our definition, we can include in it the concept of "reactive" processes only if we can exclude all purposive overtones in the idea. Despite statements to the contrary, this in my view is so

difficult that I would regard the omission of the concept as a very great advantage.

Admittedly there are some changes following injury (for example, at one extreme thrombosis and blockage of an artery and at the other the appearance of some neoplasms) which are not inflammatory; but, as was stated earlier, it is impossible to achieve a definition which is comprehensive, concise and yet sharply delimited—principally because natural processes are not like that.

Just as a complete definition of life can be made only by the inclusion of all our known observations, similarly anything short of a statement of many special features of inflammatory conditions must be open to some objections. Appreciating this, I would define inflammation as the series of changes in living tissues which follow an injury.

#### *Phenomena of Inflammation.*

We have not the time to discuss the phenomena of inflammation in any detail, and indeed it would be inappropriate to attempt this here. The general propositions therefore will be stated briefly.

In the first place, preliminary invasion of the tissues by organisms is a special problem that is not necessarily related intimately to the present questions, and indeed opens up so many fields of inquiry that it will not be considered. We shall begin from the point at which organisms have already gained entrance to the tissues.

Certain general phenomena may be observed at this stage: (i) disintegrative changes in the tissues (ranging from increased katabolism to necrosis); (ii) vascular changes; (iii) cellular changes involving both mobile and fixed cells; (iv) humoral changes.

#### *Disintegrative Changes.*

Disintegrative changes in tissues at or adjacent to an area of injury vary greatly in intensity. On the one hand there may be obvious macroscopically recognizable necrosis, and certain forms of this will be discussed later. On the other hand the tissue alterations may be so slight that to group them under this general term may seem misleading and unreasonable.

In the group of mild traumatic inflammations, the great impetus to the study of which was given by Sir Thomas Lewis and his school, there are clearly demonstrable products of tissue activity which are to be interpreted reasonably as resulting from tissue damage. Between these and the examples of indubitable necrosis all stages are to be found.

At one time it was thought that organisms were directly responsible for the inflammatory changes; but the observations just mentioned have made it clear that many of them are produced in an indirect manner. This throws a glimmer of light on the cases in which organisms, saprophytic or latent pathogenic, are present in the tissues, but as long as they produce no damage to cells no change results merely from their presence.

The breakdown of tissues is of particular importance, in that, as has been indicated, it brings all types of inflammation into line. Those which follow mechanical, chemical or thermal injuries are clearly the result of tissue injury; those due to bacterial invasion show features which are essentially the same, with some super-added phenomena. We cannot review, in the time available, the numerous clinical and experimental observations, so it must suffice to state that tissue damage is an early phenomenon in every type of inflammation, even if it occurs to variable degree among the types.

#### *Vascular Changes.*

Vascular changes are amongst the earliest, and in mild cases are the principal changes observed in an area of injury. It is scarcely necessary to say that, though all the other phenomena vary considerably in the time and intensity of occurrence, hyperæmia due to arteriolar and capillary dilatation is invariable. The various details of changes in blood flow, cellular changes *et cetera* are not discussed here. As was mentioned earlier, these changes are due to the presence of products of tissue activity or



breakdown—the principal ones being histamine and some related substances.

It should be mentioned here that this exemplifies the point made earlier regarding the teleological concept. We know that histamine, probably by initiating an axon reflex, causes capillary dilatation. We used to say that the purpose of this dilatation was to wash away toxic products. Presumably this happens incidentally, but it is foolish to regard it as the *Ultima Thule*.

The important feature of the recognition of histamine as the active agent is that the significance of the products of tissue injury is immediately emphasized, and demands, and as we shall see, is beginning to receive, some attention. Here interest is centred on the processes that may be observed rather than on some hypothetical purpose.

Accumulation of fluid in the tissues in an area of inflammation is invariable; but the amount found ranges from a negligible quantity in some cases to such an amount as to become a prominent feature in others. In some of these the fluid accumulation is directly associated with the activity of a special organism, but in other cases it is completely independent of any such factor.

Without our going into details of experiments and hypotheses, it may be accepted that, in a general way, factors determining fluid accumulation are similar to those producing non-inflammatory oedema. Briefly, these are changes in the permeability of the vascular channels, alterations in the relative intravascular and extravascular pressures and in the osmotic pressure of the tissue fluid (and the accompanying changes in the cells of the tissues), and obstruction of lymphatic vessels. Though there may be discrepancies in some of the observed details and differences in opinion regarding them, the general principles are clear.

#### Cellular Changes.

Cellular changes have attracted attention ever since the first microscopic observations were made. Although all the cells of a tissue play some part in the process, the wandering cells, particularly those of the polymorphonuclear type, have received most notice. Their migration towards the site of injury (in most circumstances) and the phagocytosis of bacteria gave rise to the immediate assumption that they were responsible for the localization of an infection and destruction of the organisms.

For a considerable time the belief in the leucocyte barrier and in the "reaction" of these phagocytic cells was the horizon. However, many observations beyond this have gradually been collected. Thus the cells may be seen to collect when there are no organisms—for example, in a turpentine abscess. The phagocytes will engulf, in some circumstances, materials other than bacteria. It has been shown that the movement of cells is due probably to surface tension changes, and at least in part to the presence of electrical charges on the cells.

Observations such as these and the deductions drawn from them have helped to clear away the obfuscation which has arisen from terms such as chemotaxis. Terms of this kind are usually, at their inception, useful and instructive; but they are apt gradually to become meaningless catchwords. This is particularly true when they develop a thoroughly undesired and unnecessary vitalistic tone. So here again, by the replacement of "chemotaxis" by precise observations and clear-cut deduction from these, the vagueness and withal finality of the idea have been shattered, and the newer attitude should be a stimulus to further progress.

In some cases the wandering cells are few in number, while in others they are numerous. It is noteworthy that the number is necessarily related neither to the intensity of vascular effects of the infection nor to the rate of spread or localization. The problem of the influence of generalized blood-stream infection, for lack of time, will not be discussed here.

The cell which predominates in acute infections is the polymorphonuclear leucocyte; but it is noteworthy that the mononuclear leucocyte frequently precedes the former, and sometimes as in typhoid infections continues as the important cell. It is clear that there is a more or less

specific stimulus for the aggregations of each kind of cell, and these are waiting discovery.

Proliferation of the fixed cells, both of the vessels and of the intervascular connective tissue, plays an important part in all but the earliest stages. The close association of these cells with certain of the mobile cells, and indeed the transformation of one into the other, provide an elementary but important example of the capacity of cells for activities which are not apparent in normal circumstances and which used to be regarded as lost.

#### Humoral Changes.

Humoral changes are numerous and of very complex character. Recent work has shown that there are many more factors at work than had been considered previously. In passing we should note that here, more than in any other part of our subject, the teleological point of view has been haunted. It imbues every part of the subject, and the whole terminology of this section emphasizes it incessantly with terms such as immunity, antibody of this or that type, and so on. Probably it will be some time before a less romantic and artificial terminology is employed.

The formation of antibodies is not always regarded as being an essential part of the inflammatory process. Our attitude will depend on the restrictions placed on the range and scope ascribed to the process of inflammation; but since they often play a significant role in the process they must be considered.

Antibodies<sup>1</sup> are formed in various places. Some develop in tissues away from the locally affected zone, principally arising in cells of the reticulo-endothelial system. Others (including some of these just mentioned) are produced in the regional lymph nodes. Still others are formed in the local tissues. We need not stop here to raise the question (at present unanswerable) whether the cells responsible are the local counterpart of the reticulo-endothelial system or are any or all of the connective tissue cells.

The nature of the various antibodies, though fairly clear in some cases, is obscure in others, and the mode of formation is quite uncertain. Observation of flakes of protoplasm being thrown off from cells has been suggested as the morphological component of the process, but this requires further confirmation. Some of the antibodies are globulins or related to them, so though they do not fall within the range of ordinary vision it seems probable that electron-micrography may give us some information before long.

A group which deserves special consideration is that of the antienzymes. These form a large proportion of the antitoxins. Many of these are well known, even if their nature is still uncertain. Some naturally occurring antienzymes have as their prototype lysozyme described by Fleming. The observations published relatively recently by Haas<sup>2</sup> open up a specially important field; he describes an antinvasin together with other enzymes produced both by bacteria and in the tissues and discusses their action on each other. The important point is that these substances form an elaborate toxin-antitoxin complex, in which what is toxin and what antitoxin depends on the point of view. This is reviewed later.

We do not need to discuss in detail here the various forms of antibody—agglutinins, bacteriolysins, antitoxins and the like. In due course their detailed features, including their chemical nature, will be understood; but in the meantime we must group together "substances" that are related principally if not only by our teleological views concerning them.

In the foregoing a condensed statement of the important changes in inflammation has been given. This has been provided to give us a foundation on which to build our subsequent discussion. In addition an attempt has been made to emphasize the necessity for an objective outlook, and to make clear, should it be necessary, the manner in

<sup>1</sup> The term antibody is employed here to designate the various substances, changes in tissue equilibrium (with the bacteria) or other cellular alterations to which the general term has been given. It is used as a temporary expedient, and not because there is necessarily justification for the anthropocentric idea implied in the prefix "anti".

which all our ideas have been subservient to the teleological viewpoint.

#### Special Phenomena.

There are several circumstances in which special features are observed, and these deserve detailed consideration.

1. Gross destruction of tissue occurs in some cases—for example, in gas gangrene infections, in some staphylococcal infections and in some "synergistic" infections.

There can be no question but that the condition here is associated directly with the presence of a particular organism, and that the death of tissue is due, directly or indirectly, to the action of chemical substances produced by organisms. In the first type the nature of the toxic agent is well known, and the effect is directly on the tissue cells. In the second case the tissue necrosis is associated with vascular changes—thrombosis is usually apparent—so that the effect, at least in part, is indirect. In the third group possibly both factors are operative.

One further form of tissue destruction, often associated with bacterial infection, occurs as an allergic phenomenon and is discussed shortly.

2. Spread of infection is a common accompaniment of the inflammatory process. Very often this is slight, but in some cases it is a striking and indeed all-important feature. It can be induced experimentally by the introduction of a "spreading factor" now known to be an enzyme designated hyaluronidase. First observed to be present in testicular extract, it has been found in spider venom and has been discovered in streptococci, some gas-forming organisms and some staphylococci amongst other organisms.

3. Localization of infection is a commonly observed but important and special phenomenon. The process is clearly very complex. It has been suggested that the precipitation of fibrin due to the action of coagulase, blocking the lymphatics, plays some part. The agglutination of bacteria, making of them particles which are too large to pass readily along tissue spaces, is another. Inhibition of enzyme activity, dilution of toxins by accumulated fluid and destruction of bacteria must also be significant. In addition it is probable that still other unknown factors are important.

These special features, chosen as the most arresting of their kind, have been discussed briefly to emphasize that they are not to be regarded as due to peculiar changes nor as explicable by differences of "tissue reactions". They are the result of the same kind of changes as occur in the more usually observed and thus the more "typical" forms of inflammation.

#### Allergy.

No general review of any aspect of inflammation would be satisfactory without some statement of the bewildering problem of allergy. The term has come to embrace so many different conditions that it is unlikely that any sort of order will be produced from the present chaos for some time.

Here we shall discuss only those conditions which arise in association with some kind of bacterial infection. We may include rapidly developing forms of tuberculosis and similar conditions, and if you will allow some assumption, acute rheumatism, *polyarteritis nodosa* and the like.

These conditions, as opposed to the large class due to poisons, dusts and many chemical substances, fall into certain distinct pathological groups.

1. In one group there are a variable degree of hyperaemia and usually a relatively gross amount of fluid in the tissues. This is shown specially in some skin affections and some conditions of the respiratory and alimentary canals. It is common to find an excessive number of oxyphile leucocytes.

2. A second group is characterized by death of tissue or gross interference with tissue function and can be subdivided into two parts. (1) There are some characteristic conditions, such as *polyarteritis nodosa* and *lupus erythematosus disseminatus*, in which changes in the vessels compel attention. In others, such as *erythema nodosum*,

there is an inflammatory change in the subcutaneous tissues which is associated with and apparently secondary to changes in the vessels. In this type the degree and rate of tissue damage appear to be due almost entirely to an accident—that the structures supplying the tissues with their nutriment should happen to be affected. (2) In this type there are several unrelated but histologically similar conditions. Some examples of hyperactive forms of tuberculosis and necrotic lesions seen in rheumatoid arthritis (in the periarthritic nodules) show characteristic features. The lesions of acute rheumatism sometimes resemble these, but also show features of the vascular group.

The intention here is not to discuss these conditions in detail, nor to suggest that we have adequate knowledge of their morphology, but to indicate that they show general features of inflammation. It is apparent that amongst the allergic conditions we have conditions that have very little connexion with each other. Nevertheless they fall into fairly well defined pathological groups, even if from other points of view their nature is obscure.

#### Interpretation of Changes in Inflammation.

The numerous, varied and variable changes indicated above are due to a complex series of interrelated causes, but these can be arranged in several fundamental groups. Doubtless in due course others will be appreciated; but in the present state of our knowledge the known phenomena may be considered under the following mechanisms: (i) the action of products of tissue damage; (ii) the action of bacterial products; (iii) the action of immune bodies; (iv) the action of tissue enzyme systems.

1. During the brief review of changes found in inflammatory conditions, given above, some of the deductions that have been drawn were mentioned in passing. It may be noted that the literature in this field, particularly from the biochemical point of view, is becoming large and correspondingly difficult to encompass. This is in part because numerous observations are being made without elaboration of adequate coordinating or integrating principles. Thus only a small part of the subject can be dealt with and many omissions are recognized.

It is clear that in non-bacterial inflammation the action of histamine and related substances has been established. The evidence is sufficient for us to accept the view at least tentatively that this applies also to bacterial inflammation. The bacteria thus, for the most part though not entirely, produce their changes in the tissues in an indirect way. First there is damage to tissue cells, and the product of this damage in its turn gives rise to the phenomena, vascular and cellular, which constitute the principal phenomena of inflammation.

In the last few years the original work of Lewis has been extended and amplified by Menkin. Menkin has extracted from tissues and tissue fluid in inflammatory conditions a series of chemical substances. Some of these, after adequate chemical treatment, have been obtained in crystalline form. These substances, when reintroduced into the body, give rise to certain definite effects, and accordingly they have been named "leukotaxine", "leucocytosis producing factor" ("L.P.F."), "pyrexin", "necrosin" and "leukopenic factor".

We owe a considerable debt to Menkin<sup>10</sup> and other workers in this field, in that they are beginning to place the many phenomena of inflammation on a sound pharmacological basis in place of the vague concept of "tissue reactions" of previous decades. However, the grave disadvantage, which, as was mentioned earlier, appears to be inevitable and inherent in all such work, is that there is a certain finality about the substances described—and this is emphasized by the names given to them. What we must remember is that the identification of these substances is not an end in itself but is merely a stepping stone to further progress.

Further investigations have been made in this direction, and various relatively simple substances have been suggested as being responsible for the vascular and cellular phenomena. These require confirmation; but the present rate of accumulation of observations suggests that



before long these substances will be distinguished clearly. One difficulty is that, in all probability, there are quite a number of them, and that they vary in amount and kind in different cases.

Though details are uncertain, the general principle is clear—that a considerable number of the changes in inflammatory conditions are due to the presence of isolable products or groups of products of cellular damage.

2. Bacterial products are of great importance, and consist of the actual protoplasm of the organism itself and various substances (toxins) produced by the organism, liberated and acting independently of it. Though the bacterial protoplasm may be significant in some special cases, the toxins produced are overwhelmingly more important in the vast majority of cases, so that they will be discussed here.

The bacterial toxins may be divided at the moment into two main groups: those whose action is well known and fairly well understood—these are the enzymes—and those whose nature is not well known. Almost certainly some members of this second group before long will be transferred to the first, but there are some which appear to have a different mode of action.

The enzymic nature of some bacterial toxins has been recognized now for nearly two decades. As was stated previously, this was appreciated first with the "spreading factor" hyaluronidase. Since then a large number has been investigated, including a toxin of *Clostridium welchii*—lecithinase, coagulase, collagenase, fibrinolysin, and hemolysins amongst others. Their names are descriptive and indicate the nature of their activity. In addition other enzymes such as lipase have been observed.

Most organisms possess a collection of these enzymes, and in many cases the virulence depends on the activity of a group of them. Apart from the cumulative effect of several enzymes, it has been shown that one may facilitate and augment the action of another. This is illustrated by the effect of lipase on the rate and degree of action of hemolysin.<sup>10</sup>

The action of these enzymes has been studied *in vitro*. When those produced by an organism have been investigated, the effect on the tissues can be prognosticated with some confidence. This has been done with remarkable accuracy in some cases; thus it has been demonstrated that the *in-vitro* observations give a clear idea of the nature of the changes occurring *in vivo*.

One of the important implications of these observations is that the various changes—necrosis, spread of infection, local blood destruction and similar changes, which were attributed to variations in resistance of the individual or an essential part of the "reaction"—are now known to be due to the "virulence" of the organism. We are on the path to understanding what was previously expressed by merely another vague catchword.

The second group of toxins comprises a number whose action is known to the extent that they cause a specific type of cellular damage. They include such as the toxin of the staphylococcus, and the toxin of the diphtheria bacillus. In addition there are some which are not peculiar to a specific organism but have a particular action—for example, destruction of leucocytes (leucocidin). As has been stated, some of these may turn out to be enzymes, but it is probable that some are not. It is not proposed to speculate further here.

3. Immune body production is very well known and in recent years has been becoming more clearly understood. Ehrlich's ideas of the processes were "diagrammatic and picturesque" and influenced almost all subsequent thought, and the original notions have been modified only in details. A great deal of work has been done on these details and there are disagreements regarding some of them, but the general conceptions remain.

As the result of the action of foreign material on body cells, substances<sup>1</sup> are produced and liberated which in one

way or another make the original substance inert. This phenomenon in its various forms—precipitation, agglutination, solution of solid material (as with bacteriolysins)—has been thoroughly studied. No special statement is practicable in a short space here.

It is necessary to mention once more the question of allergy. Under this appellation, as suggested previously, there is a large more or less loosely related fraternity. It is proposed, not to discuss the many general phenomena, but to suggest that local changes which are of different types are grouped together because their severity is so much greater than would seem warranted by known circumstances.

In some cases the phenomena appear to be due to an unusual amount of antigen and antibody, and the changes such as edema and hyperemia are commensurate with this. In other cases the destructive changes are due to the accident of the involvement of the vessel walls in an inflammatory process. In still others the large amount of tissue death suggests the action of an antibody to the tissue's own cells. In this regard the paper by Gell, Harington and Rivers<sup>11</sup> is most instructive and opens a new field of inquiry. Whatever we may think of any of these details, the general situation is clear.

Until about 1924 the severity of allergic lesions and the destruction of tissue were regarded as an inexplicable paradox. Then Opie<sup>12</sup> put forward the suggestion that it was a particularly strong reaction of the tissues which, though associated with death of tissue was nevertheless—possibly because of this—a much more efficient localizing and "defensive" mechanism. This of course was seized on and has been accepted until recently, when it has been attacked by Rich, who has shown that such a suggestion cannot be supported by experiment—indeed, is disproved.

Here again we see that the changes of an allergic nature should not be regarded as some aberrant form of "reaction", but rather as a variant (however poorly understood) of the changes which follow an injury to the tissues.

4. Tissue enzymes belong to different groups which have a different significance at different times in the inflammatory process. (i) The normal enzymes of cells of course have the double action of synthesis and breakdown of chemical substances, and the direction of the action depends on various physico-chemical factors. At the death of cells, provided the enzymes are not destroyed immediately, these cause autolysis of the tissues. This effect is seen best in suppurative states, and the liberation of proteinase by leucocytes is one important example of this action. (ii) Various antibodies to various bacterial enzymes occur in the tissues. Some develop after the introduction of the bacteria, but others appear to occur independently of this.

Haas<sup>13</sup> has shown that the tissues possess an enzyme which he terms antinvasin. Invasin<sup>14</sup> is a term coined by him as a synonym for hyaluronidase. He has shown that the presence of antinvasin neutralizes the action of invasin or hyaluronidase (hence its name), and thus prevents the spread of infection. What is significant is that he has shown that organisms produce another "substance" which neutralizes antinvasin. This he designates proinvasin.

The principal reason for mentioning this work is that here is an example of an organism developing an antibody to tissues—indeed "reacting" to the products of tissue activity. It is clear that if we should be inclined to favour the old ideas of "reaction" to injury, we are in a quandary as to whose reaction we are to consider—should it be that of the body or that of the bacterium? If we are to be just and reasonable we must consider both, and when we do, then I feel that we have arrived at that satisfactorily detached viewpoint whence, without undue thalamic activity, we can examine phenomena and critically assess their value.

<sup>1</sup>That various "antibodies" are merely names given to phenomena and not necessarily substances is expressed in the recognition of a precipitin, an agglutinin, an opsonin and a lysin as being merely different activities, in various circumstances, of a single antibody.

<sup>11</sup>It is appreciated that the introduction of names such as these adds nothing to our knowledge of the subject, and indeed they are likely in due course merely to augment our array of catchwords. They are mentioned here, not because they are intrinsically desirable, but because they do emphasise a useful point of view.

## Conclusion.

In résumé, we observe that in bacterial infection there is a close and complicated association, almost a blending, of two living organisms. The changes which occur range from cellular proliferation on the one hand to death and disintegration on the other, and these occur in both bacteria and body cells. Some of these changes, though of great biological importance, do not come within the scope of this discussion; but it is clear that in the host's tissues there are changes which have very different origins.

The phenomena of inflammation are complex vascular and cellular changes. Many of these are the result of alterations in the tissues themselves, and may be regarded as the "reaction" of these tissues. There are others, however, which are the result of the direct activity of bacterial products—for example, spreading factor or hyaluronidase—and these changes cannot be reasonably regarded as due to a tissue reaction. Thus, if we include these in the scope of the changes of inflammation (and it is difficult to see how they can be excluded), then, as was stated previously, "reaction" is too narrow a term for a satisfactory definition. Inflammation should be regarded as the series of changes following injury.

## Epilogue.

To say that there are processes, other than those mentioned here, which we still do not visualize is mere platitude, but none the less true. However, even if we do not comprehend more than a few of the complex processes which constitute the phenomena of inflammation, it is apparent that the older idea of "localization" of infection as being the result of some simple "reaction" of tissues is grossly inadequate. Localization of infection is the incidental result of numerous intricate and many-sided processes.

If I seem to have laboured some of the points in this discussion overmuch, I can only say that my experience has been that it is usually difficult to make brief but at the same time clear statements which involve the contraversion of established notions. These ideas usually are so intermingled with every part of our philosophy that, should it become necessary to attempt to eradicate them, this must be done piecemeal, and unfortunately this demands repetition.

In conclusion, let me say what is apparent to you all, that in every part of this subject there are many problems that we could and perhaps should have discussed. However, from our present point of view the medley of phenomena can be reduced to a relatively few groups which, though complicated, are governed by certain well-defined general principles.

The advances of the last few years have been remarkable, and have shown that despite innumerable difficulties our understanding of the phenomena is gradually becoming clearer. To quote Longfellow's "Michael Angelo":

There are great truths that pitch their shining tents  
Outside our walls, and though but dimly seen  
In the gray dawn, they will be manifest  
When the light widens into perfect day.

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## THE ELECTRICAL STIMULATION OF MUSCLE AND NERVE.

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I HAVE chosen for my subject tonight one which I feel offers more difficulties to the physiotherapist than most. Moreover, it is one in which considerable advances have been made in the last few years, and the end is not yet. Many of our ideas already need revising, and I feel sure that the next few years will see even greater changes.

It is essential first to consider some of the problems of electrophysiology. Having studied the production of electrical potentials in the tissues, we shall then be in a better position to interpret the effects on the body of electrical currents introduced from outside.

During muscular contraction, a small part of the energy becomes manifested as an "action current". The electrocardiograph is used to study these action currents produced during contraction of heart muscle. It has also been shown that local injury to tissue results in what is called an "injury current" and experimental work has led to an explanation of these phenomena.

All living cells are surrounded by a membrane. In the case of resting nerve and muscle, a state of permanent polarization exists, the inner or intracellular side of the membrane being lined with negative ions, while on the outer side there are positive ions. Action currents produced during muscular contraction are presumably due to a migration of negative ions through this membrane to the exterior. Local tissue injury results in rupture of this membrane, and again there is a migration of negative ions from inside the cell to the exterior. These electrical and ionic concentration changes are apparently found in all living phenomena. Starling puts it in a nutshell when he says that "every beat of the heart, every twitch of a muscle, every stage of secretion of a gland, is associated in the same way with electrical changes".

Voluntary muscular activity is always of a tetanic nature; that is, before the muscle can relax after the stimulus is applied, another stimulus is thrown in, and as a result the muscle stays contracted. These impulses are sent out from the Betz cells in the cerebral cortex, along the motor pathways to the muscles concerned. Moreover, they are discharged in volleys, and different motor units in a muscle contract at different times. This asynchronous activity is a feature of normal muscular contraction, and is an amazing provision of nature to enable the muscle to maintain tension steadily.

Having briefly reviewed these biophysical phenomena, let us now study the application to the body of electrical currents from outside, for the purpose of stimulation of muscle and nerve. W. Nernst in 1903 first propounded the theory that such stimulation was due to changes in ionic concentration at the cell membrane.

In the testing of the electrical reactions of muscle and nerve, the oldest and still the most useful routine method is the use of galvanic and faradic current. Galvanic or direct current produces a stimulus only at make or break—that is, when there is a change in ionic concentration. In faradic current we have 100 potential peaks a second, each peak acting as a stimulus; as a result the muscle is kept in a state of tetanic contraction as long as the current flows.

The reliability of electrical tests depends largely on the experience of the operator, together with the most meticulous attention to detail.

Normal electrical responses are as follows.

In the muscle test, the faradic current causes a quick contraction which persists as long as current flows, and ceases as soon as current ceases. Galvanic current causes no contraction while the current is flowing steadily; but there is a quick twitch at make and break: kathode closing contraction → anode closing contraction → anode

† Abridged from a paper read at the Australian Physiotherapy Association Congress at Adelaide, March, 1948.



opening contraction → kathode opening contraction. With both faradic and galvanic currents the contraction is greatest when the active electrode is placed over the motor point of the muscle, corresponding to the entry of the main nerve into the muscle. This is usually at the middle of the fleshy belly of the muscle—that is, at the junction of the proximal one-third and distal two-thirds of the muscle.

In the nerve test, stimulation of the nerve trunk produces similar responses in the muscles supplied distal to the point of stimulation.

Abnormalities in electrical responses may be classified as quantitative changes and qualitative changes.

Quantitative changes are not of great significance. Increased excitability is found in upper motor neuron lesions (for example, hemiplegia), in various nervous diseases, and in the early stages of a lower motor neuron lesion. Diminished excitability is found in cases of disuse and wasting of muscles from various causes.

Qualitative changes are of great importance.

The myotonic reaction is found in Thomsen's disease, and here we find that with faradic stimulation the muscles stay contracted for some time after the current is turned off.

The myasthenic reaction characterizes *myasthenia gravis*, and here with faradic stimulation the muscles tire very quickly and cease to contract after a few stimuli have been applied. Unfortunately this reaction is often not manifest until relatively late in the disease, when the diagnosis can be made on clinical grounds alone.

The most important changes are those found in the reaction of degeneration. A lower motor neuron lesion is followed by Wallerian degeneration, and concurrently with the pathological changes, abnormalities develop in the electrical responses known as the reaction of degeneration. This reaction is found only in an organic lesion of the lower motor neuron and is an important diagnostic feature of such a lesion.

Let us consider such a lesion—for example, a peripheral nerve injury. During the first few days the only change is hyperexcitability. Gradually there develop the signs of the reaction of degeneration, and fourteen days after the lesion these changes are fully developed. Testing should therefore be performed after this lapse of time.

There are various degrees of the reaction of degeneration. Absolute reaction of degeneration is found only in long-standing cases of complete lesions, in which the muscle has become largely fibrosed. It is characterized by complete absence of response of muscle or nerve to either faradic or galvanic current.

Complete reaction of degeneration is found in complete lower motor neuron lesions. There is no response to faradic or galvanic stimulation of the nerve trunk. Stimulation of the muscle with faradic current evokes no response, but galvanic stimulation produces a typical sluggish contraction. The strength of the contraction is of minor importance; the essential feature is the slow worm-like contraction, as opposed to the almost instantaneous twitch that occurs in normal responses. In complete reaction of degeneration there may also be an upset of the formula, and anode closing contraction may be greater than kathode closing contraction. There may be a longitudinal reaction, in which the contraction is greatest when the active electrode is placed over the end of the muscle, and not over the motor point.

Partial reaction of degeneration is found in incomplete lesions, during the development of complete reaction of degeneration in progressive lesions (for example, pressure from a tumour or abscess), and during recovery from a complete lesion, as the reactions gradually return to normal *pari passu* with regeneration of the nerve.

There are many forms of partial reaction of degeneration, and it is unnecessary to try to memorize them all.

If reaction of degeneration is present, and if it does not conform to the clearly defined types of either absolute or complete reaction of degeneration, then it is partial. All that is necessary, therefore, is to define what constitutes evidence of the reaction of degeneration. The most important sign is the sluggish galvanic response,

and this alone is certain evidence of the reaction of degeneration.

An upset of the formula, together with the longitudinal reaction, is evidence of the reaction of degeneration. Neither of these on its own is sufficient without further evidence.

Electrical testing therefore gives valuable information.

(i) The presence of the reaction of degeneration is evidence of an organic lower motor neuron lesion. In paralysis due to other causes (for example, hemiplegia, hysterical palsy) the reaction of degeneration is not present. (ii) Electrical testing determines the extent of the lesion—partial or complete. (iii) It determines the site of the lesion. Reaction of degeneration will be found in those muscles supplied distally to the lesion, whereas those supplied proximally to the lesion will have normal responses. (iv) It is of value in prognosis. Absolute reaction of degeneration indicates a hopeless outlook as far as recovery is concerned. Partial reaction of degeneration indicates a better outlook than complete reaction of degeneration. Repeated examinations are of considerable value. The prognosis is bad if complete reaction of degeneration persists for long; nevertheless if regeneration must occur over a long distance, many months may elapse before there are clinical or electrical signs of recovery. If reaction of degeneration gradually becomes more complete, it indicates a progressive lesion, and the possible necessity for surgical intervention. If, on the other hand, the reactions move back towards normal, recovery is indicated.

Deiherm and Nion in Paris have recently extended the scope of the galvanic and faradic test by means of the "Diagnoflux", in which the galvanic and faradic thresholds are estimated.

There are other methods of electrical testing. The condenser method has not proved of great value; but determination of the chronaxie is of value, as it is greatly lengthened in cases of reaction of degeneration. The chronaxie method is tedious; but is of particular value in following progress, as the result is recorded as a mathematical figure. Moreover, the personal factor is largely eliminated, and different technicians should all obtain the same figure.

The complete scheme for testing may be summarized as follows: (i) clinical examination, (ii) galvanic and faradic test, (iii) determination of threshold, (iv) if necessary, chronaxie testing.

Apart from testing, electrical stimulation is of great value in treatment. What are the indications for this treatment?

1. Electrical stimulation is useful in muscle wasting and weakness due to disuse, when the reactions are normal. Even when the patient can voluntarily contract his muscles, the use of stimulation as an adjunct to active exercise will often greatly accelerate recovery. An outstanding example of this is the use of faradic foot baths for flabby flat feet. In other cases—for example, immobilization after fractures—the patient cannot efficiently exercise himself, and here stimulation is particularly valuable. The early institution of this treatment at the outset, while the patient is still immobilized, is a valuable preventive measure against the rapid wasting which often occurs.

2. Adhesions can sometimes be loosened by the use of electrical stimulation to produce vigorous muscular contraction.

3. Reeducation is an indication only too often neglected. In the reeducation of muscles, a few minutes spent on stimulation are often invaluable in teaching the patient how to use his muscles. In hysterical or functional paralysis, stimulation is of course a *sine qua non*, and the result is often dramatic.

4. Peripheral vasomotor disturbances such as chilblains are often relieved by stimulation, with the resulting increase in muscle tone.

5. Causalgia is sometimes helped by stimulation.

6. Stimulation has some use, as in the Bergonie chair, for the treatment of obesity.

7. Last, but not least, comes the important group of lower motor neuron lesions, including peripheral nerve injuries and Bell's palsy. The recent work at Oxford has proved that in peripheral nerve injuries, the early and frequent use of stimulation prevents wasting and fibrosis in the affected muscles so that when regeneration of the nerve has occurred the muscle is capable of functioning in an efficient manner. Once fibrosis is allowed to occur, it is irreversible and causes permanent incapacity.

Faulty technique is responsible for much of the criticism of the results of stimulation; yet the problem is simple if certain basic principles are observed. What are these principles?

1. Always employ the most comfortable current which will evoke a contraction.

2. Avoid overting the muscle at all costs.

3. Ensure a satisfactory contraction of the muscle.

The first problem is obviously the choice of current. The currents available are galvanic, faradic and rapid sinusoidal, the last-mentioned being a 50 cycle alternating current. In order to stimulate the muscle and to give it periods of rest, these currents must be either interrupted or surged, by hand or automatically. In each case the surged form is more comfortable, but a less powerful stimulus than the interrupted form. Galvanic current offers the most powerful stimulus, but is much less comfortable than the other two. As far as treatment is concerned, faradic and sinusoidal currents behave similarly and may be used interchangeably, the choice depending largely on the apparatus available and on the personal preference of the operator. Both these currents, particularly in the surged form, produce contraction with little discomfort.

These currents may be placed in order as follows: (i) surged sinusoidal or faradic; (ii) interrupted sinusoidal and faradic; (iii) surged galvanic; (iv) interrupted galvanic. The higher in the list, the more comfortable the current, but the less powerful the stimulus. We use the most comfortable current which will evoke a satisfactory contraction; thus in muscle wasting with normal reactions we use surged faradic or sinusoidal, whereas in complete lower motor neuron lesions we must use interrupted galvanic in order to get a response.

Other currents are occasionally used. The current from a static machine is used to produce vigorous contractions in order to loosen adhesions, while the galvanic current may be modified in certain ways. The Leduc current is a galvanic current interrupted at a variable frequency—as high as 100 per second—while at the same time it is possible to vary the ratio of active and inactive periods. A ratio of one active period to nine rest periods is valuable in the treatment of causalgia.

In the Lapicque current the interruption is made gradual by the use of shunt condensers, and this current is sometimes preferred in the treatment of cases of the reaction of degeneration.

An interesting development is the recent production of the balanced pulse current. In the treatment of peripheral nerve lesions with galvanic stimulation, dermatitis is a not uncommon complication. This is apparently an ionic effect, and is prevented by reversing the current after each stimulus. This reverse current is too weak to act as a stimulus, but is passed for a correspondingly longer time, so that the total ionic movement in each direction is the same. This balanced pulse current promises to be useful in such cases.

Once the current has been chosen, what dosage is to be employed? The current should be sufficient to produce a satisfactory contraction with the minimum of discomfort, and treatment should be given at least two or three times a week, and if possible daily in the early weeks of peripheral nerve lesions. The duration of each treatment is of paramount importance. The cardinal principle is to stimulate each muscle effectively, but at all costs to avoid fatigue. Over-treatment, with the production of fatigue, is responsible for many of the poor results of treatment by electrical stimulation. The signs of fatigue are (1) the contraction becoming weaker and

more sluggish, (ii) the occurrence of tremor during treatment, and (iii) discomfort following treatment.

I feel this lecture would be incomplete without some reference to electromyography, which in recent years has permitted further study of nerve lesions. By the insertion of a screened coaxial hypodermic needle electrode through the skin into a muscle, it is possible to study action potentials. With the aid of an amplifier these may be converted into sound, which may be heard through a loud speaker; alternatively they may be studied visually on a cathode ray oscilloscope.

In the normal resting condition, no electrical activity can be found in voluntary muscle. During voluntary contraction, motor unit action potentials appear, taking the form of spikes with an amplitude of 100 microvolts to one millivolt, and a duration of five to ten milliseconds. They are heard in the loud speaker as low-pitched sounds which vary in number and frequency with the strength of the contraction. Normally these different motor units in a muscle manifest asynchronous activity. It has been shown that in poliomyelitis, synchronous activity of different motor units is a bad sign. Further, in poliomyelitis simultaneous activity may occur in opposing muscle groups.

In denervated muscles, in place of motor unit potentials we find fibrillation action potentials. These are of two kinds: those caused by insertion of the electrode, which last only a few seconds; and those which are spontaneous and occur rhythmically at a rate of two to ten per second while the needle is motionless in the muscle. Both types are of one or two milliseconds' duration and up to 100 microvolts' amplitude. They are heard in the loud speaker as sharp clicks.

During regeneration of a peripheral nerve, fibrillation action potentials diminish before return of motor unit potentials, and as fibrillation diminishes, motor unit activity increases as recovery occurs. Small polyphasic motor unit action potentials often occur during this stage of recovery.

Synchronous motor unit activity, which often occurs in poliomyelitis, is not found in peripheral nerve lesions, and appears to be characteristic of intramedullary lesions.

#### Conclusion.

In conclusion, I hope that even if the picture I have painted of this subject should appear a little blurred in places, you may perhaps forgive me if I have given you a few glimpses of the fascinating ramifications of this branch of your work—a branch which is not static, but is in a state of active evolution.

#### TRANSUTERINE INJECTION OF LIPIODOL IN THE TREATMENT OF STERILITY.

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The investigation and treatment of married couples who have been unable to produce progeny have been dealt with extensively. This article refers particularly to the therapeutic value of hysterosalpingography, but in my series of cases this method of therapy has not been used until the simpler avenues have been explored. These simpler investigations are frequently overlooked, and in many cases patients are subjected to tubal insufflation by the method of Rubin, or to the instillation of iodized oil into the uterus and Fallopian tubes, while actually the male member may be the whole cause of the childless marriage. In one such case the wife had been treated for endocervicitis, tubal obstruction and malposition of the uterus (the latter by abdominal section); but in the final investigation of the husband, who had not been examined previously, it was found that he had complete aspermia due to a gunshot



wound received in the first world war, the wound having probably severed his seminal vesicles from the urethra. Complete sexual potency and vigour were present, but spermatozoa were not found in the semen.

My series of cases is not large, but it does give an opportunity of deciding the value of hysterosalpingography with lipiodol in the treatment of sterility.

Rubin,<sup>11</sup> in 1920, performed transuterine insufflation for the treatment of sterility in women with occluded Fallopian tubes. Rubin introduced a volumometer and also a kymograph which, as it revolved, registered the pressure in the tubes. The gas used was carbon dioxide, and the maximum level to which the pressure was permitted to ascend was 200 millimetres of mercury.

Over the past eighteen years, both at the Royal Adelaide Hospital and in private practice, I have tended to place less reliance on carbon dioxide insufflation of the tubes, and to use the transuterine injection of iodized oil into the tubes for better results. The reason for this change is because tubes which have appeared to be impervious to carbon dioxide have become patent with the use of lipiodol. The injection of lipiodol allows a series of X-ray photographs to be taken, and if, as is frequently found, there is a blockage at the fimbriated end of the tube, then the possibility of successful salpingostomy can be assessed. When the obstruction is cornual, then operation is out of the question except for intrauterine implantation of an ovary. In some cases the outline of a submucous fibroid is found, which previously has not been recognized. I have had many cases in which pregnancy has occurred subsequent to the injection of oil through uterus and tubes, although these patients have remained sterile after carbon dioxide insufflation. There appears to be less reaction from lipiodol than from carbon dioxide; this may be due to the small antiseptic effect of the iodized oil. The shoulder pains also, which are due to the irritation of the diaphragm, do not occur after the injection of lipiodol.

In 1941 Leventhal and Solomon<sup>12</sup> produced some excellent results from the treatment of sterility by hysterosalpingography.

In 1936 Francillon-Lobre and Dalsace<sup>13</sup> recorded hysterosalpingography in 585 cases collected over ten years. Of these, 434 patients had patency of one or both Fallopian tubes and 89 conceived. The authors further concluded that if a sterile woman had one tube patent, she had one chance in five of becoming pregnant after the transuterine injection of lipiodol into the tubes.

In a series of patients treated by hysterosalpingography, Robins and Shapiro<sup>14</sup> examined 330 sterile subjects, with the result that 32% became pregnant.

Beclere and François<sup>15</sup> had 18% of cases in which pregnancy occurred.

Braut and Tizon<sup>16</sup> had 26% of cases in which pregnancy subsequently occurred.

Schulze<sup>17</sup> published reports of 25% of his series in which pregnancy occurred.

In the last 150 cases of my own series there were 21 in which complete obstruction was found, and among these, one woman, who had been sterile for five years, became pregnant in twenty-one weeks. This introduces the question whether the lipiodol may have any solvent effect on the occluded tubes. Of the remaining 129 patients who had either one or two tubes patent after hysterosalpingography, many had been found by Rubin's method to have occluded tubes. Of these 129 patients, 43 were later known to have become pregnant, while many of the others were lost to the records, and whether they were subsequently sterile or fertile is unknown.

In this series, then, it is known that of those who were investigated by this means, 25.5% became pregnant, and of the 129 patients who had partially or wholly patent Fallopian tubes, 33.3% were known to have become pregnant.

In view of the facts and findings of other workers in this direction, it would appear that the iodized oil accomplishes something more than the mere mechanical forcing out of tubal adhesions *et cetera*. Writers have shown that something like 15% of subjects whose Fallopian tubes have been impervious to both gas and lipiodol have sub-

sequently become pregnant after the latter method of treatment, although the hysterosalpingogram gave completely negative findings.

The methods which I have adopted and associated with a general survey of the wife and the husband are as follows.

The woman is first examined, to see whether there are any abnormal factors associated with her general health. The possibility of endocrine dyscrasia is investigated, and finally a careful pelvic examination is made so that any uterine irregularity either in position or in configuration is ascertained, and the adnexa are examined carefully also.

The cervix is next inspected through a bivalve speculum, and any erosion or endocervicitis is noted for treatment. If all the details required are found to be satisfactory, then an attempt is made to insufflate the Fallopian tubes, but only in the intermenstrual resting stage of the endometrium. In Rubin's test, should the gas not pass through the tubes at a pressure of 200 millimetres of mercury after the tubal peristalsis and spasm have been allowed to pass off, then the husband is sent to a urologist for the investigation of the uro-genital system, a count of the spermatozoa and an estimation of abnormal forms. If the number, shape and motility of the spermatozoa are satisfactory, then a hysterosalpingogram is proposed for the wife.

The time for this investigation is on the eleventh or twelfth day after the onset of menstruation, when the cycle is of the normal twenty-eight day type. The method adopted is as follows. The vagina is cleaned thoroughly through a self-retaining vaginal speculum, and the cervical plug is removed on a probe containing *Liquor Potassae*. Here it must be stated that neither before the performance of Rubin's test nor before the transuterine injection of lipiodol into the Fallopian tubes should preinvestigational coitus be encouraged. Some writers suggest that coitus should take place just prior to the examination; but this method does not appear to be free from infective factors, and certainly the pregnancy results do not proclaim the advantage of this method, which to some people may be repugnant.

After the removal of the cervical plug the cervix is swabbed with "Merthiolate". This helps to sterilize the area, and the "Merthiolate" colour does not absorb the light. A uterine sound is next introduced to ascertain the length and direction of the uterine cavity. Finally a long cannula, with the intrauterine end slightly curved and swelling to a large metal shoulder about one and a half inches from the uterine end, is introduced. The shoulder of the cannula is pressed against the cervix and so makes it watertight. A tenaculum now seizes the posterior cervical lip, and by an attachment on the cannula the tenaculum holds the shoulder of the cannula against the *portio cervicis*. About four millilitres of lipiodol are injected into the uterine cavity, and the first X-ray picture is taken. If the lipiodol is finding its way into the Fallopian tubes a further two or three millilitres are injected and another X-ray picture is taken. The lipiodol may now be at the fimbriated end of the tube, but not obviously passing into the peritoneal cavity. In this case a further one or two millilitres of lipiodol are injected and a swab on a sponge-holder is placed in the posterior fornix; if this swab is massaged on either side and counter-massage is applied from the abdomen at the same time, the lipiodol may be seen in a further X-ray picture to have passed into the peritoneal cavity, and actual peritoneal "wash" is begun. This massage of the lateral fornices is regarded, in this series, as having a good effect upon the occluded fimbriated end of the tube.

The pH of the vagina is estimated in some cases, and before coitus Ringer's solution, as produced under the name of "Nutri-sal", is injected into the vagina in order to increase and encourage and lengthen the life of the spermatozoa motility.

#### Discussion.

Hysterosalpingography usually gives much more information than insufflation, and if the subjects are carefully selected, is attended with no greater risks. In several cases the Fallopian tubes were found to be patent when

the oil was injected, although gas could not be forced through.

Oil appears to release adhesions and straighten out kinks of the tubes, and the oil remaining seems to produce a more permanent result. In several cases of uterine retroversion, although the tubes were impervious to gas, they were distended and made permeable by oil. The retroversion appears to kink the tubes, and, after a while, the kink becomes permanent, owing to the shrinkage of the mesosalpinx.

Restoration of complete patency in diseased Fallopian tubes has been produced, and tubal peristalsis in these cases appears to have been restored. This increased muscular activity also increases the possibility of fertilization.

#### Summary.

1. The result of the uterine injection of lipiodol by Tizon's method in 150 cases has resulted in 43 pregnancies.

2. Hysterosalpingography by means of lipiodol under pressure has yielded better results than the intratubal insufflation of gas as in Rubin's method.

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### ADDISON'S DISEASE: REPORT OF A CASE WITH UNUSUAL FEATURES, AND REVIEW OF THIRTY CASES.

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ADDISON'S DISEASE is described as having certain predominant symptoms and signs, which include "(1) asthenia and fatigue, (2) pigmentation of the skin and mucous membranes, (3) anorexia, nausea and vomiting, (4) loss of weight, (5) hypotension and small heart, (6) dizziness and syncopal attacks, (7) decreased resistance to cold (hypometabolism), (8) collapse with dehydration and circulatory failure".<sup>(1)</sup> The diagnosis is held to be confirmed by certain alterations in the blood chemistry, the characteristic findings being a lowered serum sodium level and a raised serum potassium level.<sup>(2)</sup>

A case is described below of a young woman who presented certain of the features of Addison's disease—asthenia, pigmentation of the skin, and gastro-intestinal disturbance—but in whom the blood pressure was normal, there was no loss of weight, and the blood chemistry was normal as regards the concentrations of serum sodium and potassium. Since X-ray examination revealed bilateral calcification in the suprarenal areas, and the Mantoux test produced a strongly positive result, there was strong evidence of tuberculosis of the suprarenal glands. About the same time, another young woman was admitted to the Royal Melbourne Hospital with a somewhat more characteristic picture of Addison's disease, arterial hypotension being added to the features described in the first

case, but again with absence of significant changes in the serum levels of sodium and potassium. Both patients improved under treatment with adrenal cortical hormone.

The findings in these two cases suggested a review of the cases of Addison's disease recorded at this hospital, particularly to determine which of the "characteristic" features were most frequent and hence the most valuable in diagnosis, and also what reliance could be placed on the biochemical findings in diagnosis.

Some difficulty was experienced in deciding which cases to accept as of Addison's disease. This is not synonymous with tuberculosis of the suprarenal glands, because the latter is found fairly commonly *post mortem* without the clinical picture of Addison's disease. The diagnosis is essentially clinical; but the presence of all the characteristic features in the one case is exceptional, while each of the features individually may be caused by some other disease. Pigmentation of the skin and asthenia were the most constant clinical features in the cases diagnosed as of Addison's disease in the hospital records. The criteria adopted in selecting cases for this review were the presence of both these features, neither being accounted for by any other condition, along with the presence of at least one other of the characteristic features listed above. It is realized that these criteria may be criticized on the basis that the cases have been selected, as in a large series of cases in the literature pigmentation is described in only some 95% of cases. However, it was considered necessary to adopt such criteria to avoid the inclusion of cases other than Addison's disease. Other cases were excluded because of inadequacy of the records. There remained from 1923 to 1947 inclusive records of thirty cases for analysis.

#### Report of a Case.

Mrs. A.C., aged twenty-eight years, was admitted to the Royal Melbourne Hospital on May 7, 1947. Of her five children, ranging in age from eleven to two years, four were well, while one had died from pneumonia when aged three and a half months. From the birth of her third child, six years previously, her skin had become increasingly dark. During each of the succeeding pregnancies the pigmentation rapidly deepened, being noted chiefly about the mouth and forehead. She had suffered from bronchitis during each of the two winters preceding her admission. For three months she had experienced "fainting turns". She did not fall or lose consciousness during the attacks, but became short of breath, felt her heart beating, and "did not seem to have the strength to expand her lungs". Her weight had remained constant. The appetite was good. She was troubled with eruptions after the "fainting turns". Vague abdominal pain with nausea had been present for one week prior to her admission to hospital. Diarrhoea "easily came on"—for example, after eating sweets.

On examination, the patient was a somewhat thin, dark-skinned young woman. The brown pigmentation was generalized, but more prominent about the forehead and mouth. There was no pigmentation of the buccal mucous membrane. The arterial blood pressure was 125 millimetres of mercury (systolic) and 85 millimetres (diastolic). No abnormalities were detected in the heart, lungs, abdomen or nervous system. The patient's weight was eight stone and half a pound.

Special investigations carried out while she was in an out-patient clinic awaiting admission to hospital resulted as follows. The serum sodium content was 341 milligrammes per 100 millilitres. The serum potassium content was 22 milligrammes per 100 millilitres. X-ray examination of the chest revealed that the lung fields were clear. X-ray examination of the suprarenal areas revealed calcification of both suprarenals. Calcification was observed in the left side of the middle portion of the abdomen, probably a gland. The Mantoux test produced a positive ("+++") result with 0.1 millilitre of a 1/100 strength of old tuberculin. Examination of the blood gave the following information: the haemoglobin value was 11.2 grammes per 100 millilitres, the erythrocytes numbered 4,700,000 per millilitre, and the colour index was 0.85; the leucocytes numbered 6000 per cubic millimetre; no abnormalities were seen in a blood film.

Further investigations on the patient's admission to hospital gave the following results: the serum sodium content was 352 milligrammes per 100 millilitres, the serum potassium content was 20 milligrammes per 100 millilitres, the fasting blood sugar level was 0.1 gramme per 100 millilitres, and the blood urea content was 34 milligrammes per 100 millilitres.



The response to treatment was as follows. Hypodermic injections of distilled water given daily to note any psychological effect produced no improvement. She was then treated by the addition of salt to the diet and the ingestion of an extra six grammes of sodium chloride per day. She was given a hypodermic injection of ten milligrammes of "Percorten" and the following day one millilitre of "Eschatin", the dose of the latter being increased by one millilitre per day until a dose of five millilitres was reached. Thereafter, she was given five millilitres of "Eschatin" by hypodermic injection twice a week. This treatment produced great improvement, and by May 18, 1947, the patient was feeling "really well". On July 27, 1947, the serum sodium content was 400 milligrammes per 100 millilitres, and the serum potassium 21 milligrammes per 100 millilitres. The treatment has been continued since the patient's discharge from hospital, and she has remained well. The pigmentation is unaltered.

#### Clinical Features.

In the thirty cases of Addison's disease analysed from the hospital records there were nine male patients and twenty-one female patients.

The earliest age of onset was nineteen years and the highest sixty-nine years, the average being forty-two years. In fifteen of the thirty cases the age of onset was between forty and sixty years.

The frequency of the individual features in these thirty cases is shown in Table I.

Thus, next to asthenia and pigmentation of the skin, which have been taken as essential criteria to the accepting of the diagnosis in this series, loss of weight and gastro-intestinal symptoms were the most frequent features. The weight loss was usually considerable, a loss of one or two stone in twelve or eighteen months being a common

TABLE I.  
Clinical Features in 30 Cases of Addison's Disease.

Clinical Feature.	Number of Cases.		
	Present.	Absent.	Not Recorded.
Asthenia .....	30	0	0
Pigmentation of skin .....	30	0	0
Loss of weight .....	27	2	1
Gastro-intestinal symptoms .....	26	2	2
Arterial hypotension:			
Systolic pressure less than 100 millimetres of mercury .....	19	11	0
Diastolic pressure less than 65 millimetres of mercury .....	13	14	3
Pigmentation of mucous membranes .....	14	6	10
Dizziness of syncopal attacks .....	5	0	25

recording. The greatest weight loss was four stone in eighteen months. Of the gastro-intestinal symptoms, anorexia and vomiting were more frequent than diarrhoea.

#### Biochemical Changes.

Estimations of the serum sodium and potassium contents were carried out in this hospital only from 1941 onwards, and are available for only ten cases of this series. The biochemical determinations in these ten cases are summarized in Table II.

The normal range of the serum sodium and serum potassium contents used in this table is based on determinations of the values for these substances in a control series of forty healthy adults by Miss Beryl Splatt, of the biochemical department of the Royal Melbourne Hospital.

It is to be noted that in the small series of cases of Addison's disease in which these determinations were made, the only change of sufficient frequency to be significant is the lowering of the serum sodium level. In only three of the ten cases were the changes sometimes considered characteristic of Addison's disease present; in the three cases in which the serum potassium level was raised, the serum sodium level was also raised.

After treatment with adrenal cortical extract or desoxycorticosterone acetate, the serum sodium level rose in all cases, whereas the serum potassium level, if originally outside normal limits, tended to return to a normal level.

It was not possible to point to any characteristic difference in the clinical features as between those cases in which the blood chemistry was altered from those in which it was normal. The three patients whose serum sodium content was not lowered were all young women.

#### Morbid Anatomy.

In only nine cases of the total series are post-mortem reports available. In five of these cases the suprarenal glands were affected by caseating tuberculosis; in the other four they were atrophic. In all cases the pathological condition was bilateral, and both the cortex and medulla of the glands were involved, being either wholly or almost wholly destroyed.

#### Treatment.

No analysis of the effects of various types of treatment will be attempted. However, it is of interest to follow the introduction and development of specific therapy for this disease.

TABLE II.  
Biochemical Determinations in 10 Cases of Addison's Disease.

Blood Constituent.	Number of Cases.			
	Raised.	Lowered.	Normal.	Not recorded.
Serum sodium content (normal: 315 to 360 milligrammes per centum) .....	0	7	3	0
Serum potassium content (normal: 15 to 26 milligrammes per centum) .....	3	2	5	0
Fasting blood sugar level (normal: 70 to 110 milligrammes per centum) .....	0	4	5	1
Blood urea level (normal: 20 to 40 milligrammes per centum) .....	3	0	4	3

In the early records there is no mention of a specific treatment, and the results are consistently bad.

The first note of the use of suprarenal cortical extract in the series was in 1935, when a patient was treated by the administration of extra sodium chloride together with injections of "Eschatin" with a favourable response.

The use of the synthetic preparation desoxycorticosterone acetate first appears in 1940, when, in the treatment of a patient previously given injections of "Eschatin", the latter was replaced by "Percorten" and the improvement was maintained.

Treatment by the implantation of "Percorten" tablets was carried out in one case in 1945. Although the patient was at first kept in reasonable health by this method, sudden death followed a second implant. In another instance a patient's condition was stabilized on "Percorten" injections, and then a "Percorten" tablet was implanted. The patient became comatose and there was a sudden rise in blood pressure. The tablet was removed, but the patient died eight days after the implantation. Hence, treatment by this means may not be without danger.

One patient was treated in 1946 by injection of fetal adrenal into the sternum, as advocated by Thiersch;<sup>(3)</sup> but as the patient left for another State there is no record of the result.

#### Discussion.

The diagnosis of Addison's disease is notoriously difficult. It is suggested by the combination of certain clinical features already listed, and is made more certain if there is evidence of tuberculosis of the suprarenal glands.

The reliance sometimes placed on the blood chemistry to confirm the diagnosis would appear from the small series presented in which such investigations were carried out to be ill-founded. If the serum sodium level is lowered, this is confirmatory evidence of Addison's disease, but the latter may be present with a normal serum sodium level. The level of the serum potassium would appear to give no help in the diagnosis.

The recognized difficulty in the diagnosis of Addison's disease has led to the development of special tests; but

these have disadvantages which limit their value. The test of Cutler, Power and Wilder,<sup>(4)</sup> depending on the continued high concentration of sodium and chloride in the urine in spite of a diet low in salt, would appear to be a reliable test for the presence of supranal insufficiency; but the danger of precipitation of a crisis is a deterrent to its frequent use in suspected cases of Addison's disease. The "water test" of Robinson, Power and Kepler,<sup>(5)</sup> which combines three disturbances that may occur in Addison's disease—decreased urea clearance, increased chloride clearance, and disturbed excretion of water—is without this disadvantage, but is not uniformly reliable, as it is found not to give positive results in all cases of Addison's disease, and to give positive results sometimes in other conditions.<sup>(6)</sup>

#### Summary.

A case of clinical Addison's disease with normal blood chemistry is described.

The cases of Addison's disease recorded at a public hospital between the years 1923 and 1947 are reviewed with regard to clinical features, biochemical changes, morbid anatomy and treatment.

The relative importance in the diagnosis of the clinical features, blood chemistry and special tests is briefly discussed.

#### Acknowledgements.

It is a pleasure to acknowledge my indebtedness to Dr. Ivan Maxwell for permission to publish a case history, to Dr. Keith D. Fairley for advice concerning the preparation of this paper, to Miss Beryl Splatt, of the biochemical department of the Royal Melbourne Hospital, for all the biochemical determinations, and to Miss A. Haile, of the records department of the hospital, for searching out the histories.

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#### VALUES FOR THE MINERAL CONTENT OF THE SERUM OF AUSTRALIAN ADULTS.

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In considering the results of analyses performed on the blood of patients, one is often faced with assessing the significance of small deviations from the normal figures. For such a problem the average figures usually given are useless, the range of normality being essential to an understanding of the readings. Also, although it is probable that the chemical composition of the blood is the same in the Australian as in the English or American citizen, this has been assumed rather than investigated.

A. J. Barnett's investigation of cases of Addison's disease at this hospital, published in this issue of the journal, once again drew attention to the lack of such data, and it seemed desirable to publish these values.

The figures given below were arrived at partly with the above end in view and partly during the course of another investigation.<sup>(1)</sup>

#### Method of Analysis.

Potassium was estimated in the serum by Kramer's method,<sup>(2)</sup> the maximum error found being 3.3%. Certain precautions are necessary in the collection of blood for analysis for sodium or potassium. Potassium is present in the red cells of the blood in a concentration of approximately 400 milligrammes per centum, and in the plasma in a concentration of 20 milligrammes per centum, and after blood is shed potassium rapidly leaks from the cells into the plasma or serum. The potassium content of one specimen of plasma one hour after collection was 26.4 milligrammes per centum, and seven hours later the level when red cells and plasma were left in contact was 38.9 milligrammes per centum; seven days later it was 76 milligrammes per centum. It must be remembered that this transfer of potassium from the red cells takes place without laking of red cells, and a specimen some hours old without evidence of haemolysis must be discarded,<sup>(3)</sup> Jeanneney and Servant<sup>(4)</sup> and later Scudder, Drew, Corcoran and Bull<sup>(5)</sup> being amongst the observers of this fact. If there is any evidence of haemolysis in serum or plasma initially, the result obtained from the specimen will be valueless.

Specimens of blood for this analysis must, therefore, be collected with a dry syringe, without any trauma from a tourniquet adjusted too tightly; the blood must be forwarded to the laboratory immediately and in the laboratory the serum must be separated from the clot within one hour. As the interchange is less in clotted blood and no error is introduced from the anticoagulant, it is preferable to use serum for the analysis.

The sodium content was estimated by Butler and Tuthill's<sup>(6)</sup> modification of Barber and Kolthoff's<sup>(7)</sup> method. This method was accurate to 0.6%. Sodium is present in greater amount in the serum than in the red cells, as shown by Hald,<sup>(8)</sup> the difference being as three to five. Interchange takes place more slowly than in the case of potassium, but the precautions described above must be observed.

The method of estimation of the calcium content was that of Kramer and Tisdall.<sup>(9)</sup> The maximum error was 0.93%.

The content of magnesium was estimated on the fluid decanted from the calcium oxalate precipitate as described by Denis.<sup>(10)</sup> The magnesium was precipitated as ammonium magnesium phosphate, and after washing, estimated as phosphate by Kuttner and Lichtenstein's method.<sup>(11)</sup> This method was found to be accurate to 1.0%.

The chloride content was estimated by Van Slyke's method<sup>(12)</sup> and was accurate to 0.5%. This element is unequally distributed between serum and red cells, and will undergo changes in distribution on storage, the chloride passing from the serum or plasma to the clot or red cells. The syringe for collection of blood must not be rinsed with normal saline solution.

#### Procedure.

By the courtesy of the Honorary Director of the Red Cross Blood Transfusion Service, specimens of blood were obtained from twenty male and twenty female donors. These donors had all been passed as medically fit, and all had a haemoglobin content of their blood of at least 85% (14.0 gramme standard). Their blood pressure was within normal limits. The specimens of blood were collected with the precautions described above.

The results of the individual analyses are shown in Table I.

#### Discussion.

Table II shows the average values obtained from these analyses in milligrammes per centum and in milliequivalents per litre, and also the range of values.

Two of the female donors gave high values for potassium—namely, 25.6 and 26.4 milligrammes per centum, the figures being confirmed on a later occasion.

Marinis, Muirhead, Jones and Hill<sup>(13)</sup> give a table of normal ranges by various authors and methods; the present range is wider than that of the majority of these observers, but agrees with the values of Marinis, Muirhead, Jones



TABLE I.

Potassium, Sodium, Calcium, Magnesium and Chloride Contents of the Serum of 40 Healthy Adults (Milligrammes per Centum).

Number of Subject.	Potassium.	Sodium.	Calcium.	Magnesium.	Chloride.
Males.					
I ..	21.3	326	10.1	2.40	365
II ..	24.1	341	9.6	2.16	369
III ..	18.1	341	9.9	2.32	356
IV ..	18.5	341	9.6	2.30	341
V ..	19.7	336	9.4	2.14	372
VI ..	20.2	329	10.4	2.08	359
VII ..	19.0	334	9.5	2.35	335
VIII ..	18.4	342	11.5	2.38	377
IX ..	22.4	329	10.9	2.10	369
X ..	18.3	354	11.0	2.09	356
XI ..	16.8	316	11.2	2.24	351
XII ..	20.6	339	10.2	2.50	339
XIII ..	22.9	342	10.5	2.20	342
XIV ..	18.3	343	9.9	2.18	366
XV ..	18.3	341	9.6	2.24	356
XVI ..	19.3	333	10.0	2.41	338
XVII ..	19.7	334	9.4	2.20	372
XVIII ..	18.7	338	9.9	2.21	368
XIX ..	20.2	325	10.3	2.34	357
XX ..	19.0	322	9.6	2.46	337
Average ..	19.7	334	10.1	2.26	352
Females.					
XXI ..	22.7	334	9.2	2.31	352
XXII ..	15.6	339	10.5	2.00	369
XXIII ..	19.5	329	10.0	2.01	372
XXIV ..	18.5	340	10.0	2.56	369
XXV ..	17.2	329	11.4	1.92	363
XXVI ..	21.3	342	10.0	2.16	372
XXVII ..	25.9	324	11.0	2.70	380
XXVIII ..	26.4	358	10.6	2.20	381
XXIX ..	21.4	335	10.0	2.79	337
XXX ..	22.4	348	9.1	2.10	355
XXXI ..	18.6	338	11.4	2.36	377
XXXII ..	17.2	329	11.4	1.92	362
XXXIII ..	22.4	329	10.9	2.00	369
XXXIV ..	21.4	332	10.0	2.79	352
XXXV ..	20.4	341	10.1	2.51	348
XXXVI ..	23.1	346	10.5	2.20	335
XXXVII ..	22.8	336	9.1	2.10	363
XXXVIII ..	23.0	334	9.3	2.10	357
XXXIX ..	18.5	326	11.0	2.00	360
XL ..	20.2	328	9.5	2.34	369
Average ..	20.8	336	10.2	2.27	363

and Hill obtained by the use of the flame photometer on 107 ambulatory adults (blood donors). The other observers based their series on from three to seventeen observations, with the exception of Consolazio and Talbot's<sup>(13)</sup> series of 37 adults, whose figures correspond with Marinis, Muirhead, Jones and Hill's and with those found in this series.

TABLE IIA.  
Average Values of Mineral Content of Serum of Adults.

Mineral.	Milligrammes per Centum.	Milliequivalents per Litre.
Potassium .. ..	20.2	5.2
Sodium .. ..	335.0	146.0
Calcium .. ..	10.1	5.07
Magnesium .. ..	2.3	1.9
Chloride .. ..	358.0	101.0

TABLE IIB.  
Range of Values of Mineral Content of Serum of Adults.

Mineral.	Milligrammes per Centum.	Milliequivalents per Litre.
Potassium .. ..	15.6-26.4	4.0-6.8
Sodium .. ..	310.0-359.0	137.0-155.0
Calcium .. ..	9.1-11.5	4.5-5.7
Magnesium .. ..	2.0-2.8	1.7-2.3
Chloride .. ..	329.0-381.0	93.0-107.0

The values found for sodium are in close agreement with those of the observers quoted above.

The values for calcium in serum are of interest, in that values below 9.5 milligrammes per centum were found in six of the forty persons, and the serum of only five persons had a calcium content of more than eleven milligrammes per centum. This was at variance with one's impression of the values obtained in the laboratory.

## Summary.

The potassium, sodium, calcium, magnesium and chloride contents of the serum of forty healthy Australian adults have been estimated, and the values obtained have been compared with those of other observers. The range of values found is shown with a view to assisting in deciding if small variations found are significant. This range is particularly pertinent to chemical changes in patients possibly suffering from Addison's disease.

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# HÆMOPHILUS INFLUENZÆ MENINGITIS IN FORTY INFANTS TREATED WITH SULPHONAMIDES, TYPE-SPECIFIC ANTISERUM AND PENICILLIN AT THE CHILDREN'S HOSPITAL, MELBOURNE.

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THE infants under consideration were the last forty suffering from *Hæmophilus influenzae* meningitis to be admitted to the Children's Hospital, Melbourne, prior to June 1, 1946, and before streptomycin became available for the treatment of this condition. There were five deaths in the series; in other words, one-eighth of the children succumbed to their infection. Twenty-three of the children were males and seventeen females.

These results are adduced as an earnest endeavour to demonstrate the efficacy of certain methods of diagnosis and treatment. Owing to several factors, this series is not comparable with the first forty *Hæmophilus influenzae*

TABLE I.

Benedict's Solution.	Test Tube Number.	Amounts of Cerebro-spinal Fluid Added.	Tubes are Boiled. Reaction Indicated by X.					
1 millilitre	1	0.05 millilitre	X	0	0	0	0	0
1 millilitre	2	0.1 millilitre	X	X	X	0	0	0
1 millilitre	3	0.15 millilitre	X	X	X	0	0	0
1 millilitre	4	0.2 millilitre	X	X	X	X	X	0
1 millilitre	5	0.25 millilitre	X	X	X	X	X	0
Interpretation of results			Over 50 milligrammes	40 to 50 milligrammes	30 to 40 milligrammes	20 to 30 milligrammes	10 to 20 milligrammes	Less than 10 milligrammes
			Mild infection			Severe infection.		

meningeal infections which have occurred since the introduction of streptomycin at the Children's Hospital, Melbourne, and among which there have been seven deaths.

The figure forty was chosen for convenience, and the number includes those children whose illness was diagnosed and treated according to the routine outlined hereunder.

The diagnosis of meningitis was made in all but four of these cases in the casualty department of the hospital. Frequently no clinical signs of meningeal involvement could be elicited; but if a child presented with pallor and pyrexia, persistent vomiting, convulsions, or an unusual syndrome for which no other cause could be found (the examination including ears and throat and microscopic examination of the urine), the approval of a senior resident medical officer was obtained for a diagnostic lumbar puncture. In the case of infants, and in dealing with drowsy or comatose children, lumbar puncture was performed without anaesthesia, either local or general, as it has been found by experience that the young child resents the initial prick of the anaesthetic needle equally as much as that of a fine-bore lumbar puncture needle, deftly introduced; also the spinous processes, which form important landmarks, are not obliterated as they may be after the subcutaneous injection of a local anaesthetic agent.

A few millilitres of cerebro-spinal fluid were collected in two or three test tubes; one portion was kept at blood heat, incubated, and used for attempted culture of organisms; another portion was centrifuged and the deposit examined for the number and type of cells, besides being stained by the Gram method in order to determine the presence and type of any organisms. A further quantity was used for biochemical tests. At that period, owing to pressure of work in the pathology department, only those tests indicated as a necessity for the diagnosis and treatment of the meningitis were performed. In *Haemophilus influenzae* infections, the glucose content of the cerebro-spinal fluid—since it gives an indication of the severity of infection and the required dose of antiserum—was frequently determined by the resident medical officer, who employed Benedict's solution in a simple five-tube method (see Table I). If the cerebro-spinal fluid was not crystal clear on macroscopic examination, 20,000 units of penicillin dissolved in one millilitre of normal saline solution were introduced into the theca via the lumbar puncture needle and the child was admitted to hospital. This prompt institution of therapy was undoubtedly a contributing factor in the rapid recovery of some of the children in this series, from a disease in which one hour's delay may prejudice the chance of the child's eventual complete recovery.

On the child's admission to hospital, such measures were undertaken as seemed indicated by the urgency of the situation, and treatment was commenced without delay. In most cases one of the sulphonamide drugs was administered by mouth. In this series 33 children received sulphamerazine and seven sulphadiazine.

The choice of drug was often governed by its availability at that time. Experience led us to favour sulphamerazine because an adequate blood concentration could be maintained by administration every eight or even every twelve hours; such intervals meant less disturbance for a sick child, and less work for the nursing staff. Further, it was our impression that renal complications tended to occur less frequently with sulphamerazine.

Large and prolonged doses of the sulphonamide drugs were found necessary, but in spite of this no serious toxic symptoms were encountered. Anaemia was not uncommon during the child's illness, necessitating regular and frequent haemoglobin estimation. Seven children subsequently required blood transfusions; the anaemia was probably due to the infection, but it is possible that in some instances it was brought about by small amounts of naturally occurring agglutinins, which at that time were present in the rabbit serum.

The initial dose of the sulphonamide drug used was generally three, occasionally four, grains per pound of body weight for the first twenty-four hours; this was reduced as rapidly as the clinical response permitted, the maintenance dose being approximately one to one and a half grains per pound of body weight per day. Sulphonamide therapy was continued throughout the infection, and was generally the last type of therapy to be discontinued.

As soon as the *Haemophilus influenzae* microorganisms were identified in the smear or culture, and often before their type was determined, type B specific rabbit antiserum was given by the intravenous route according to the method described in detail in a previous communication.<sup>(1)</sup> This serum was used originally at the Children's Hospital, Melbourne, by A. G. Nicholson in October, 1943.<sup>(2)</sup>

In this series 39 children received antiserum; the remaining other child died eight hours after admission to hospital, and prior to the establishment of the diagnosis. Of the 39 receiving serum, 22 children required only one dose of antiserum, usually 120 millilitres, the amount given being governed by the glucose content of the cerebro-spinal fluid in accordance with the figures presented in the following chart modified from the work of Hattie Alexander<sup>(3)</sup> (Table II).

TABLE II.

Sugar Content of Cerebro-spinal Fluid. (Milligrammes per Centum.)	Dose of Antiserum Required. (Millilitres.)
Less than 10	120
10 to 20	90
20 to 30	60
30 to 40	30
Over 40	Generally no antiserum required; infection responds well to sulphonamides alone.

If the glucose content of the cerebro-spinal fluid showed no rise after forty-eight hours, a further dose of antiserum was administered, usually intramuscularly. Two children each received four such doses of serum, and both developed mild serum rashes. Five children each received three doses of serum, and none developed serum reactions. Nine children each received two doses of serum, and four of them later developed rashes diagnosed as measles by several competent observers; there had recently been several children affected with measles in the ward. A pair of twins both contracted *Haemophilus influenzae* meningitis; both had a rise in temperature and a rash following serum therapy. All patients recovered, and apart from this and



the possible anaemia (*vide supra*) there were no serious serum reactions.

Our experience was that better results were obtained by the initial intravenous administration of serum; this may have been due in part to the preliminary four hours' treatment with 5% glucose solution in normal saline solution, the rationale of which is that the glucose increases the urinary excretion of free type-specific carbohydrate, and permits the antiserum direct access to the carbohydrate in the capsule of the organism itself. In addition it mitigates the violence of the reaction resulting from the sudden union of large quantities of antigen and antibody, and at the same time corrects dehydration.

For the more gravely ill children the administration of penicillin was continued by three-hourly intramuscular and daily intrathecal injections. Penicillin was administered to 25 children in this series for periods varying from a single initial dose up to fourteen days in one case, with an average of two to four days' administration. The intramuscular dose of penicillin varied with the age and weight of the child, according to a dosage scale presented in a previous communication.<sup>(4)</sup>

TABLE III.

Days in Hospital.	Number of Patients.
Under 1	1 <sup>1</sup>
1 to 7	3 <sup>1</sup>
8 to 14	2
15 to 21	9
22 to 28	5
29 to 35	5
36 to 49	8
Over 50	7

<sup>1</sup>Death.

At that time penicillin was not considered to exert any effect on the Gram-negative *Haemophilus influenza*, so that one was puzzled by the greater rapidity of response to therapy of those children who had received penicillin at the initial lumbar puncture; although at that time such chemotherapy seemed unscientific, its use was continued empirically because of the apparent benefit.

One child was maintained successfully with treatment by penicillin and sulphonamides for several weeks, during which interval type-specific antiserum was not available; when the intrathecal administration of penicillin was withheld the meningitis tended to relapse, and it was not until antiserum was administered intravenously that this boy completely recovered.

I later found it possible to sterilize the cerebro-spinal fluid in a case of resistant *Haemophilus influenza* meningitis with penicillin given intrathecally in doses of 100,000 units per millilitre.<sup>(6)</sup>

Within the last two years papers have been written and published by Stephen Williams,<sup>(6)</sup> by Zinnemann,<sup>(7)</sup> and by North, Wilson and Anderson,<sup>(8)</sup> demonstrating the range of penicillin sensitivity of the *Haemophilus influenza*, particularly the type B strain, which is that found commonly in meningeal infections. Heparin, 0.5 millilitre, was administered intrathecally in any case in which the

cerebro-spinal fluid was exceptionally turbid or showed a tendency to fibrin clot on standing, or in any case in which there was clinical evidence of cerebro-spinal block. In my opinion heparin has a place in the treatment of purulent meningitis; it appears to obviate cerebro-spinal block by preventing organization of the products of inflammation within the theca, and as organizing arachnoiditis about cranial and spinal nerves is an important factor in the development of paralytic sequelae, the administration of heparin seems justified, particularly as its use in the manner indicated caused no ill effect. Heparin was used for

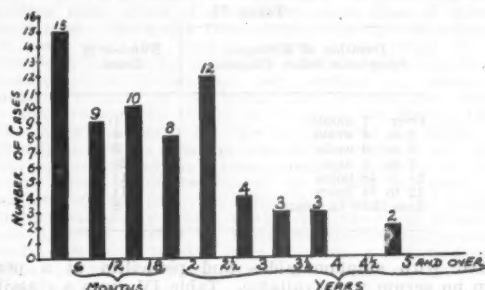


FIGURE I.

ten of these children, whose fluid was excessively turbid; there were no paralytic sequelae in the whole group.

The 35 surviving children were observed at monthly intervals for the first three months after their discharge from hospital, then at intervals of three months, and many of them up to twelve months after their illness. No untoward mental or physical sequelae were noted; the mothers frequently stated that the children had become more "nervous" than before, perhaps sleeping badly or

TABLE V.

Duration of Prodromal Signs before Diagnosis.	Number of Cases.
Over 1 month	1
2 to 4 weeks	5
1 to 2 weeks	6
2 to 7 days	0
24 to 48 hours	4

manifesting irritability and disobedience. These symptoms appeared to subside with regular small doses of phenobarbital; iron and extra vitamins seemed of value during the child's convalescence.

Supportive and adequate nursing care is imperative for success in the treatment of these children during their illness, and the services of an experienced ward sister are invaluable. The children were treated in a small, well-ventilated ward of their own; as not only did they require special attention, but by group observation and comparison of the several patients the clinician acquired an apprecia-

TABLE IV.

Name.	Age.	Duration of Symptoms.	Days in Hospital.	Comments and Post-mortem Findings.
Peter H.	5½ months	4 days.	Lived 36 days.	No response to sulphonamides and antiserum. Hydrocephalus and toxæmia at post-mortem examination.
Barbara H.	9 weeks.	A few hours.	Lived 48 hours.	Fulminant infection in a very young baby. No post-mortem examination.
Dennis R.	14 weeks.	A few hours.	Lived 8½ hours.	Fulminant infection in a very young baby. No post-mortem examination.
Alan G.	22 months.	2 days.	Lived 3 days.	Acute hydrocephalus, toxæmia, bilateral otitis media due to <i>Haemophilus influenza</i> .
Bernard O'H.	4½ months.	A few hours.	Lived 48 hours.	Fulminating infection; had bilateral mastoiditis with <i>Haemophilus influenza</i> .

tion of their response to treatment, and was the better able to estimate progress.

Table III indicates the duration of the child's illness whilst in hospital, from the day of admission to discharge. This period was extended in several instances, because of the development of intercurrent infections, or because of unsuitable home environment. Nine patients therefore were discharged home during the third week, and eight others during the sixth week. The longest stay in hospital was seventy-two days, required for a little girl who was

TABLE VI.

Duration of Meningeal Symptoms before Diagnosis.	Number of Cases.
Over 1 month .. .. .	1
2 to 4 weeks .. .. .	4
1 to 2 weeks .. .. .	5
2 to 7 days .. .. .	25
24 to 48 hours .. .. .	11
12 to 24 hours .. .. .	11
Less than 12 hours .. .. .	2

treated with sulphonamides and penicillin at a period when no serum was available. Table IV gives a classification of the five deaths occurring in this series.

In conclusion, there follow some tables of statistics and a diagram which may be of value in the diagnosis and treatment of *Hemophilus influenzae* meningeal infections. That the tables may have greater statistical value, I have added data gathered from the case histories of the twenty children previously reported in this journal<sup>10</sup> and from

TABLE VII.

Clinical Manifestations.	Number of Cases.
Fever .. .. .	32
Vomiting .. .. .	54
Drowsiness .. .. .	38
Irritability .. .. .	16
Neck stiffness .. .. .	48
Kernig's sign .. .. .	35
Pallor .. .. .	20
Headache .. .. .	3
Convulsions .. .. .	8
Rash .. .. .	2
Rhinorrhoea .. .. .	16
Cough .. .. .	8
Clinical pneumonia .. .. .	8
Diarrhoea .. .. .	3
Screaming .. .. .	10
Meningeal cry .. .. .	7
Anorexia .. .. .	11
Delirium .. .. .	4
Abdominal pains .. .. .	1
Earache .. .. .	5
Otorrhoea .. .. .	4
Strabismus .. .. .	4
Opisthotonus .. .. .	20
Sudden collapse .. .. .	1
Tense fontanelle .. .. .	16
Child "off colour" .. .. .	6
Coma .. .. .	13
Herpes labialis .. .. .	2
Photophobia .. .. .	4
"Teething" .. .. .	2
Thirst .. .. .	21
Dyspnoea .. .. .	4
Loss of weight .. .. .	1
Paresis .. .. .	1
Deafness .. .. .	1
Constipation .. .. .	7
Shivering .. .. .	3

six others, all of whom were treated at the Children's Hospital, Melbourne, prior to this series.

Figure 1 gives the age incidence, and shows that the disease is predominantly one of infancy, and rare over the age of three years.

Table V shows the duration of prodromal symptoms before diagnosis; these comprise respiratory (including ear) or gastro-intestinal symptoms, loss of weight, and unexplained pyrexia. The onset of meningeal symptoms was frequently indicated by neck stiffness, headache,

increase in vomiting or convulsions. Seven of these children showed no signs of meningeal involvement prior to diagnosis.

Table VI gives the duration of meningeal signs before diagnosis.

Table VII gives the clinical manifestations including the chief complaints. These figures are quoted accurately from accounts recorded on the history sheets of these children, but they may not present a true picture of the onset of the disease for a number of obvious, variable factors. (a) The sufferer himself was generally too small

TABLE VIII.

Temperature on Admission to Hospital.	Number of Cases.
Less than 99° F. .. .. .	1
99.1° to 100° F. .. .. .	7
100.1° to 101° F. .. .. .	7
101.1° to 103° F. .. .. .	23
Above 103° F. .. .. .	19
Not recorded .. .. .	9

or too ill to make any specific complaint. (b) The child's attendant sometimes gave a poor account of the child's illness because of poor powers of observation, grief or unfamiliarity with the details. (c) The details on the history sheet varied with the diligence and accuracy of the recording medical officer. However, some interesting points emerge from a study of this table.

Convulsions marked the onset in eight cases—that is, one-eighth of the total.

A petechial rash occurred at the onset in two fulminating cases, which suggests that *Hemophilus influenzae* septicæmia was present; this suspicion was not verified, but it is of interest to note that a petechial rash is not pathognomonic of a meningococcal invasion.

Respiratory prodromal symptoms including rhinorrhoea, cough and dyspnoea were not uncommon, and clinical pneumonia was present in eight of the children; the

TABLE IX.

Investigation.	Laboratory Findings.	Number of Cases.
Cell content: polymorpho-nuclear leucocytes per cubic millimetre.	1 to 100 cells .. .. .	5
	100 to 1000 cells .. .. .	8
	1000 to 5000 cells .. .. .	34
	Over 5000 cells .. .. .	19
Chloride content: milligrammes per 100 millilitres.	Average .. .. . 686	9
	Highest .. .. . 700	
	Lowest .. .. . 673	
Sugar content: milligrammes per 100 millilitres.	Average .. .. . 23.6	60
	Highest .. .. . 70	
	Lowest .. .. . 0	
Organisms.	Smear contained <i>Hemophilus influenzae</i> .. .. .	41
	Culture yielded <i>Hemophilus influenzae</i> , type B .. .. .	46

finding of pneumonic consolidation tends to give the clinician a false sense of security about the diagnosis, and he may overlook meningeal signs and unduly delay diagnostic lumbar puncture.

The most constant symptom was that of vomiting, which occurred in 54 cases; its association with diarrhoea may lead to an erroneous diagnosis of gastro-enteritis, unless the possibility of meningitis is kept in mind.

Fever and drowsiness occurred with frequency at the onset; this fever was that complained of by the persons presenting the child's history, and frequently the thermometer had not been used to record it.

A complaint of headache was made by only three children; this is not surprising, as it is rare for a child aged under three years to indicate any specific painful area. This is probably why the complaint of earache was made in only five instances, yet *otitis media* was not an uncommon accompaniment of the condition.



Neck stiffness, Kernig's sign, head retraction, and bulging fontanelle failed to occur in at least eighteen of the cases.

Constipation was twice as common as diarrhoea at the onset; in two cases the untoward symptoms had been attributed to teething.

Table VIII gives a record of the temperatures on admission to hospital. More than one-third of the children had temperatures elevated to between 101° and 103° F.

In Table IX are set out the cerebro-spinal fluid findings on initial lumbar puncture.

#### Summary.

The results of treatment at the Children's Hospital, Melbourne, of forty children suffering from *Hæmophilus influenzae* meningitis are given; there were five deaths.

These children were treated before June 1, 1946, and prior to the introduction of streptomycin. Their treatment consisted in the oral administration of sulphonamides and the use of type-specific rabbit and antiserum and penicillin; details of this treatment are described.

Tables are presented which are designed to be of value in the diagnosis of this type of meningitis; the tables cover (i) age incidence, (ii) duration of prodromal and meningeal symptoms prior to diagnosis, (iii) clinical manifestations, including chief complaints, temperatures on admission to hospital, and cerebro-spinal fluid findings, recorded from the clinical histories of 66 children suffering from *Hæmophilus influenzae* meningitis.

#### Acknowledgements.

My thanks are due to Dr. A. P. Derham for encouragement in presenting this paper, to Dr. Reginald Webster for many helpful suggestions, and to the honorary medical staff of the Children's Hospital, Melbourne, for permission to publish the figures.

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- (2) A. G. Nicholson: "Meningitis due to *Hæmophilus influenzae*: Review of Treatment", *THE MEDICAL JOURNAL OF AUSTRALIA*, Volume I, 1944, page 320.
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- (8) E. A. North, H. Wilson and C. Anderson: "The Resistance of *Hæmophilus influenzae* to the Action of Penicillin, with Special Reference to Type B Strains", *THE MEDICAL JOURNAL OF AUSTRALIA*, Volume I, 1946, page 626.

## Reviews.

### MALARIOLOGY.

FIFTY years ago Ronald Ross believed that he had found the means to banish malaria from the world. He had; but more than forty years of hard and too often disappointing work in the tropics brought caution, even pessimism, so that Rogers wrote that the simplicity in theory of prophylaxis against malaria was only equalled by its difficulty in practice. There were successes, some of them brilliant; but the labour was great and the costs were high, and they were microscopic specks in relation to the great mass of uncontrolled malaria. Now there are new hopes, based on wider knowledge and new means of attack; *Anopheles gambiae* has been eradicated from Brazil; the recent war has shown that malaria can be controlled on a scale undreamt of before; the new insecticides have revolutionized malariology,

as penicillin revolutionized surgery; and post-war trends are once more towards eradication as a practical policy. New work is still going on; but the end of the war marked a period, and provided an opportunity to integrate the newer knowledge and present a clear, succinct account of progress that had been achieved. This, Paul Russell, with West and Manwell, has attempted very successfully to do.<sup>1</sup>

The title "Practical Malariology" is modest, for the work is far more than a guide to the field worker and anti-malarial engineer; it represents rather, as they say in their preface, the knowledge that the authors have gained through experience, and it has the "practical" flavour that they are writing more often of what they know than of what they have read. Naturally they write from the American point of view, but the book is saved from being of purely American interest by the senior author's wide experience—he has not only visited, but also worked in, almost every malarial country in the world, and he even saw something of the problems in the south-west Pacific during the war. The American point of view is reflected in detail, rather than in principles (for example, in the regimen of "Atebrin" therapy prescribed, in a more cautious attitude to "Plasmoquine" than would be shared by British workers, and in matters of that sort), and does not impair the balance or the general utility of the work. The choice of illustrations, indeed, could hardly be more cosmopolitan—Puerto Rico, Madras, Malaya, Manila, Italy, to name a few, and on page 419 a typical Melanesian working a knapsack sprayer.

The book is in six sections. In the first, the parasites and their life histories are described, not only those from man, but the species recorded from other animals also. Particular attention being given to the pre-erythrocytic and exo-erythrocytic stages in bird malaria and their probable significance in relation to the then hidden stages in human infections. The recent discoveries of Shortt and Garnham will enable this section to be rounded off very prettily in a future edition. The descriptions are good, and the coloured pictures and some of the photographs are excellent. The section concludes with an adequate and practical account of technique in diagnosis and in experimental malaria, which is sufficiently up to date to include Hawking's tissue culture methods for studying exo-erythrocytic stages. Each chapter has a bibliography of selected references.

The second section, on the mosquito, is set out in similar form, and is equally thorough, about thirty pages each being given to morphology and bionomics, and 65 to field and laboratory methods. The keys to world species of Anophelines at the end of the book are to be taken in conjunction with this section. The chapter on distribution is not so satisfactory as the rest, so far as the Australasian region is concerned, for Weber's Line is attributed to Wallace, and *Anopheles amictus*, owing probably to an unfortunate misunderstanding when Colonel Russell was in Australia, is recorded as the probable cause of the Cairns epidemic and thus gains an unearned place in the list of important malaria vectors of the world.

The third section is given to infection in man, and is in some respects the weakest in the book. It has rather the flavour of the conventional text-book, and does not sufficiently stress such practical points as the irregularity of the initial fever in *Plasmodium vivax* infections or the great variability of those due to *Plasmodium falciparum*. In the account of immunity, too, the term "premunition" is not used as originally defined, and the fact that tolerance precedes the fully developed immunity does not seem to be sufficiently appreciated. As a result, the otherwise excellent figure on page 326 is somewhat marred because the "clinical horizon" is horizontal, when it should slope up to the right. These lapses are unfortunate, because tolerance is a striking feature of malarial infections and is epidemiologically highly significant in native children.

Whatever may be the deficiencies of the third section, they are more than compensated by the fourth, on epidemiology, and the fifth—one-quarter of the book—on prevention. Both reveal to the full the breadth and richness of Colonel Russell's experience, and both should be read and digested by every working malariologist. One might cavil, indeed, at the pseudo-mathematical way of summarizing a malarial situation, but even that has its uses, provided it is clearly understood that it is only a qualitative shorthand with no real mathematical significance. Again, the authors are a little unkind to Australia, in attributing

<sup>1</sup> "Practical Malariology", prepared under the auspices of the Division of Medical Sciences of the National Research Council by Paul F. Russell, M.D., M.P.H., Luther S. West, Ph.D., and Reginald D. Manwell, Sc.D., with a foreword by Raymond B. Fosdick, 1946. Philadelphia, London: W. B. Saunders Company, Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9½" x 6", pp. 704, with many illustrations. Price 60s.

to it (Figure 128) a higher incidence of malaria than it really possesses, but, by way of compensation, they are sufficiently up to date to make some mention of the Cairns investigations and even of "Paludrine".

The final section is a brief, practical description of therapeutic malaria.

#### VASCULAR DISEASES.

I. S. WRIGHT, of Cornell University College, has published a book on "Vascular Diseases in Clinical Practice".<sup>1</sup> It deals mainly with vascular disorders of the limbs, though the author lays stress on the importance of a wide outlook in dealing with such conditions. He gives a good general outline of the approach to these diseases, and without going into unnecessary detail; he discusses the methods of examination clinically, the apparatus commonly used in diagnosis, and the more usual symptoms and signs of arteriosclerosis obliterans and thromboangiitis obliterans. There are a number of excellent diagrams and photographs illustrating the location and the types of vascular phenomena.

Wright has more or less specialized in this kind of complaint for twelve or fourteen years, so that he has had a very considerable experience, and records some very valuable observations. For instance he mentions 70 patients in his own experience who suffered from burns of a greater or less degree as a result of the use of heat to the limbs in vascular diseases. Accordingly he states that the local use of all types of high temperature heating equipment, including hot-water bags, electric bulbs, infra-red lamps and diathermy, is contraindicated in vascular disease. He recommends the simplest forms of treatment, such as saline baths for open lesions, penicillin for infections, avoidance of tobacco, rest, intravenous injections of "T.A.B.", and the injection of tissue extracts, the latest of which is "Depropanex", an epinephrine antagonist, but not of proved value. Wright favours surgery mainly for amputations, and records many unfavourable results following ganglionectomies.

Raynaud's syndrome, scleroderma and calcinosis are described and discussed fairly fully. Concerning operations for Raynaud's syndrome the author is not particularly enthusiastic, but he does advise ganglionectomy before the symptoms and signs are too far advanced, with some hope of relief for several years. He also discusses oedema, polycythemia, thrombophlebitis and other vascular disorders.

This book gives an excellent summary of modern knowledge on vascular diseases, and no exaggerated claims are made for any particular technique. It is rather a useful summary of knowledge than an original work.

#### OUTLINE OF PHYSIOLOGY.

THERE has been a great tendency in recent years for teaching and research in animal physiology to become more human and more intimately correlated with human pathology and clinical medicine. It is just possible that in certain quarters this may go too far so that the student may not realize that physiology is fundamentally an experimental science which aims at the precision of physics. In the lamentably understaffed medical schools of Australia there should really be no choice in the nature of physiological teaching; it must perforce be a pre-clinical subject directly associated with the experiences subsequently gained in the pathological laboratory and the hospital ward. Still it is a good thing to remind the Australian medical student that there is such a thing as a basic physiology to be pursued and expounded with all the rigour of a pure science. "Outline of Physiology" by Amberson and Smith can be warmly commended from this aspect.<sup>2</sup> It is not a text-book to be used by medical students in their last year of physiological study, but they would be all the better for reading it as a preliminary as they would gain a surer grasp of the essentials. On the other hand the work is eminently suitable for those students who are not aiming at a medical qualification, but who are taking physiology as a subject

in a science curriculum. It is also a book admirably fitted for senior schoolboys and is to be emphatically preferred to the medical text-books which boys of certain schools are induced to read without adequate grounding in anatomy and histology—much to their subsequent harm when they attend university classes. The present edition of this book is the second appearing after nine years from the first and is improved in every respect. The exposition is lucid, the style is flowing and often racy, the illustrations, many of which are original, are of high quality. The treatment is scholarly and well up to date in the fundamentals of physics and chemistry as well as of physiology proper. Any criticisms we make are offered as helpful in the preparation of another edition which will assuredly be demanded. The physiology of voice and the mechanisms of the larynx have been omitted. The treatment of haemodynamics is too meagre and that fault is especially surprising in view of the fact that the authors are obviously at home in physics. Figures 154 and 155 are ascribed to Best and Taylor, but are really from Barcroft, of Cambridge. In the chapter on the kidney no mention is made of the pioneer work of Starling and Cushman. The description of the eye might well include a brief mention of myopia, hypermetropia, presbyopia and astigmatism. On page 94 there occurs the expression "the Mexican volcano of Catopaxi"; does this refer to Cotopaxi of Ecuador? In our review of the first edition attention was drawn to the slip in stating that the word molecule is derived from the Greek, and the same language is credited with the unfortunate hybrids, monovalent and divalent. Our criticism may not have been seen—at any rate it has not been taken to heart. These minor matters should not be regarded as detracting from a really fine book which will be read with pleasure and profit by the experienced physiologist as well as by the student thankful for a clarity and attractive style not always found in text-books.

#### Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"An Elementary Atlas of Cardiography: An Introduction to Electrocardiography and X-ray Examination of the Heart", by H. Wallace-Jones, M.D., M.Sc., F.R.C.P., E. Noble Chamberlain, M.D., M.Sc., F.R.C.P., and E. L. Rubin, M.D., F.F.R., D.M.R.E. (incorporating the third edition of "Electrocardiograms: An Elementary Atlas for Students and Practitioners"); 1948. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall (1941), Limited. 8" x 5½", pp. 120, with many illustrations. Price: 12s. 6d.

Includes two sections—one devoted to electrocardiography and the other to cardiac radiology.

"A Synopsis of Physiology", by A. Rendle Short, B.Sc., M.D., F.R.C.S., C. L. G. Pratt, O.B.E., M.A., M.D., M.Sc., and C. C. N. Voss, M.Sc., Ph.D., M.B., Ch.B.; Fourth Edition; 1948. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall (1941), Limited. 7½" x 4½", pp. 360, with illustrations, some of them coloured. Price: 20s.

Intended to be "a fairly full summary of modern physiology, particularly human physiology, in a small compass".

"Laboratory Technique in Biology and Medicine" by E. V. Cowdry; Second Edition; 1948. Baltimore: The Williams and Wilkins Company. London: Baillière, Tindall and Cox. 9" x 5½", pp. 685. Price: 22s.

Explanatory notes on microchemical and physical procedures and other matters pertaining to the laboratories, arranged alphabetically.

"Diseases of the Ear, Nose and Throat", by Douglas G. Carruthers, M.B., Ch.M. (Sydney), F.R.A.C.S.; Second Edition; 1948. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall (1941), Limited. 8" x 5½", pp. 356, with illustrations, some of them coloured. Price: 25s.

An English edition of the author's original work.

"Proteins and Life" by M. V. Tracey, M.A. (Frontiers of Science Series, General Editor, Bernard Lovell, O.B.E., Ph.D., F.Inst.P.); 1948. London: The Pilot Press, Limited. 7½" x 5½", pp. 178, with illustrations. Price: 10s. 6d.

Deals with the nature, structure and use of proteins, but is not intended to cover the whole field of protein study.

"Recent Advances in Respiratory Tuberculosis" by Frederick Heat, M.A., M.D., F.R.C.P., and N. Lloyd Rusby, M.A., D.M., F.R.C.P.; Fourth Edition; 1948. London: J. and A. Churchill, Limited. 8" x 5", pp. 307, with illustrations. Price: 21s.

Intended to be "a consecutive narrative with the new developments grafted upon a background of the ideas and conceptions previously held".

<sup>1</sup> "Vascular Diseases in Clinical Practice", by Irving Sherwood Wright, M.D.; 1948. Chicago: The Year Book Publishers Incorporated. 8" x 5", pp. 514, with illustrations. Price: \$7.50.

<sup>2</sup> "Outline of Physiology", by William R. Amberson, Ph.D., and Dietrich C. Smith, Ph.D., illustrated by the late Norris Jones and William Loechel; Second Edition; 1948. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" x 6½", pp. 518, with illustrations, some of them coloured. Price: 37s. 6d.



# The Medical Journal of Australia

SATURDAY, DECEMBER 25, 1948.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

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## ADESTE FIDELES.

AFTER an interval of several years Christmas Day falls this year on a Saturday, the day of the week on which this journal is published. There can be few people today who have not at some time or other, perhaps many years ago, asked themselves what Christmas means, or rather what it is supposed to mean. But men and women of the present day are not different from those of days gone by in that they are creatures of habit about most of the things that they do, and Christmas, like many other events, comes and goes and is often taken for granted as a reason for a holiday and an occasion for merry-making and as nothing more. Habit, being a twin sister to familiarity, may not always breed contempt, but it does imply a ready, perhaps an unthinking, acceptance of things and happenings, a dulled sense of appreciation and a forgetfulness of significance. Acceptance may be ready and appreciation may be dulled because the action in question has been taken after deliberation in the past and been shown to have a good result or at least no unfavourable sequel. Habit is a great advantage to man; in fact it may often be his salvation. Habit is described as a condition of body or mind and especially as one that has become permanent or settled by custom or persistent repetition. In zoology and botany the term habit is applied to instinctive actions of animals and to tendencies of plants. A habit may be deeply ingrained, but it can be checked or changed. In this regard it is of interest to recall that a habit is a term sometimes applied to certain forms of clothing—we speak of a riding habit or of the habit of those who live in a monastery. Let us then return to Christmas and to the fact that, though people may occasionally think about it, many give it no thought or take it for granted. The present object is to disturb this habit and to inquire what Christmas should mean to us and to others and how we stand in relation to it.

The word Christmas means the Mass of Christ and it is celebrated in the Christian Church as the festival of the nativity of Jesus Christ. The "Encyclopædia Britannica"

tells us that Christmas was not among the earliest festivals of the Church and that before the fifth century there was no general consensus of opinion where it should come on the calendar—on January 6, March 25 or December 25. The earliest identification of December 25 with the birthday of Christ was in a passage, otherwise unknown and probably spurious, of Theophilus of Antioch (about A.D. 180). The first certain mention of December 25 is in the calendar of Philocalus, A.D. 354. We read that in Britain December 25 was a festival long before the conversion to Christianity, for Bede relates that "the ancient people of the Angli began the year on Dec. 25 when we now celebrate the birthday of the Lord; and the very night which is now so holy to us, they called in their tongue *modranecht* (*mōdra niht*), that is, the mother's night, by reason we suspect, of the ceremonies which in that night-long vigil they performed". In England the observance of Christmas was forbidden by Act of Parliament in 1644; Charles II revived the feast. At the present time the real purpose of Christmas is best shown in the festal celebrations of the Christian Church. The singing of carols (the history of which, though full of interest, cannot be related here) and the giving of presents from friend to friend, with feasting and merriment, are part of our usual observance of the Christmas season. Even those who do not worship the Babe of Bethlehem or pay no heed to the teachings of the Babe become Man, often speak of Christmas as a time of peace and good will—in fact the terms are almost interchangeable—and this must be the central theme of this discussion. Music in some form is generally associated with important human occasions, and of all Christmas melodies probably none is so widely known as the old eighteenth century tune set to the words "Adeste fideles". The words are a call to the faithful to come and worship. Everyone, even those opposed to the Christian religion, will agree that to have an ideal and to do nothing about it, is stupid. To worship does not end with adoration; adoration must be translated into deeds. It is not the function of this journal to advocate belief in Christianity or the leading of a Christian life; it is, however, consistent with the journal's functions to remind all who regard the Christmas season as one of peace and good will that these are objects for which all the "faithful" should strive to the utmost—the "faithful" in this case being all those who are concerned with the welfare of the nations and of the people comprised by them.

Everyone will agree that the present are times of turmoil and threatenings, of disaster and disappointments; any morning newspaper gives evidence of this, the horrors more often than not being all paraded on the front page. It seems that all the forces of strife and of evil combine to intensify our gloom and add to our misery. The people of good will never seem to give any sign that they have joined, or even are prepared to join, hands. There are without doubt many more persons than we suppose who have good will, whose hearts are in the right place, who think of others besides themselves and show their good will in many different ways. The pity of it is that they seldom come together and that when they do the event passes unnoticed because it is not sensational and so is not "news". There is today a curious unwillingness among all kinds of people to show that they are different from the trouble makers, that they are men or women of

good will. For this all kinds of reasons may be given. To counteract it we should advance the contention previously put forward in these pages in the course of a discussion on democracy, that it is fundamental for every member of a democratic community to make some contribution to the common welfare and not to be content to spend the whole of life receiving what democracy has to give. Those who do this are the "fideles", the faithful. When we think of peace we perhaps look forward to the time when man shall neither "hurt nor destroy", when:

The wolf also shall dwell with the lamb, and the leopard shall lie down with the kid; and the calf and the young lion and the falling together; and a little child shall lead them.

And the cow and the bear shall feed; their young ones shall lie down together: and the lion shall eat straw like the ox.

And the sucking child shall play on the hole of the asp, and the weaned child shall put his hand on the cockatrice' den.

If that state or anything remotely approaching it is to come, it will be because people of good will have brought it about. It will be the work of the many and not of the few—it will be the summation of small effects and not the outcome of one *tour de force*. Everyone who puts his mind to it can do something to spread good will. Everyone has his or her sphere of influence—some spheres are small, others large—and we know that "he who is faithful in that which is least is faithful also in much". There is no need to attempt to catalogue spheres of influence; each reader can do this for himself, and medical folk will no doubt find for themselves more than one sphere in which they can achieve something. It need hardly be mentioned that efforts will be sterile if they are coloured by hopes of self-advancement. The Christmas season is the time when thoughts may be turned in this direction, for some to make a start, for others to do more than they are doing. In proportion as we try to spread our good will we shall gain the right to be numbered among the *fideles*, and when more is required of us we shall each be able to make reply at once: "Adsum."

### Current Comment.

#### INFANTILE GASTRO-ENTERITIS TREATED WITH STREPTOMYCIN.

PRELIMINARY REPORTS have been made of the treatment of infantile gastro-enteritis with streptomycin, but the most impressive information on the subject has just appeared in a paper by Ursula James and Ivor R. H. Kramer, of the Princess Louise Children's Unit, Saint Mary's Hospital, London,<sup>1</sup> based on the treatment of 30 patients with streptomycin by mouth. The patients were in three groups: four from an outbreak of epidemic diarrhoea of the newborn, four from an outbreak of gastro-enteritis in a residential nursery, 22 from the Children's Unit, including patients critically ill on admission and those not responding to routine treatment. The only factor in selection seems to have been the fact that patients treated in each respective group were those most severely ill or those not responsive to routine treatment. Routine treatment in all cases, except for patients of the third group who were critically ill on admission to hospital, consisted of an initial period of starvation for twenty-four hours, during which sterile water alone was given by mouth, followed by the gradual building up of milk feeds at the rate of 60 Calories a day. When indicated, saline solution with glucose was given intravenously,

supplemented, if administration was for longer than twenty-four to forty-eight hours, by protein hydrolysate solution. The streptomycin was given by mouth before each feed in equally divided doses. After experiments with dosage in the first two cases, a standard dose was adopted of 2.0 grammes in seven days: 0.5 gramme in the first twenty-four hours and 0.25 gramme in each subsequent twenty-four hours for a further six days. It was found that the children having streptomycin tolerated milk foods well and that these could be increased at the rate of 100 Calories a day. When streptomycin was started during the later stages of routine treatment, no further period of starvation was necessary and the feeds could be increased at the rate of 100 Calories a day from the level already reached. Of the 30 patients, 28 responded satisfactorily, the most striking results occurring in those critically ill, in those with recurrent diarrhoea and vomiting, and in neonatal gastro-enteritis. Vomiting ceased early, weight was rapidly gained, the appetite returned, the stools improved, and there was almost immediate improvement in the general condition. The streptomycin produced no evident toxic effects. The two cases of failure were in an infant, aged nine days, who collapsed and died during treatment, and in a child with bilateral mastoiditis who recovered after suitable surgical treatment; the importance of treating associated parenteral infection is stressed, as well as the danger that pathogens remote from the gut may be rendered streptomycin-resistant by the small amount of streptomycin that enters the blood stream. The investigation was started with the intention of treating gastro-enteritis associated with *Proteus vulgaris* in the stools, but it was found that patients with stools not containing this organism responded equally well. However, it is accepted by these investigators as not likely that all types of gastro-enteritis of unknown aetiology or those of virus origin will respond to streptomycin given by mouth. One notable result in this series was the shortening of the course of the disease, the usual time of discharge from hospital being nine to fourteen days after the start of treatment, even for those with very severe conditions. The value of this in reducing pressure on hospital beds and lessening the risk of cross-infection needs no emphasis. Although this is not a large series it is difficult not to be impressed by the detailed clinical reports, and this is reinforced by the statistical analysis by P. Armitage, of the Medical Research Council Statistical Research Unit, with which the paper concludes. Armitage assesses the figures coldly and pronounces that "in view of the fact that the most serious cases were chosen for streptomycin treatment, we can safely say that the results indicate a real improvement in the treated groups". James and Kramer seem to have produced results that at least warrant attempts at confirmation; while streptomycin is certainly not a drug to be used indiscriminately, confirmation will be awaited with much interest.

#### ABNORMAL PERIODS OF GESTATION.

THE possible limits of the period of gestation, while of considerable interest clinically, may be vital medicolegally. *The Lancet* has drawn attention<sup>1</sup> to a report in *The Times* of July 9, 1948, of the case of Hadlum versus Hadlum, in which the husband petitioned for divorce on the ground that, owing to non-access, he could not have been the father of his wife's child and therefore that the wife must have been guilty of adultery. The period between the last opportunity of insemination by the husband and the birth of the child was 349 days. Medical evidence was given that "the period, however unusual, was not impossible"; the court refused to infer that adultery must have occurred, and the petition failed. It is pointed out that this decision adds another three days to the period accepted as not impossible in the case of Wood versus Wood last year. In that case, in which desertion was the primary issue, the husband claimed that as the last date of actual cohabitation was August 8, 1945, and a child was born on July 20, 1946, that is, 346 days later, his wife must have committed

<sup>1</sup> *The Lancet*, October 9, 1948.

<sup>1</sup> *The Lancet*, July 17, 1948.



adultery, and so he was not bound to continue cohabitation. There was no evidence whatever of association with other men, named or unnamed. Local magistrates said that adultery was a serious allegation and it required proper proof; they could not assume that the time was impossible. Lord Merriman later in the Divisional Court upheld their decision, although the stated period of gestation was 15 days longer than the period of 331 days allowed in a judgement of Lord Birkenhead in 1921 to which Lord Merriman referred. In that case (*Gaskill versus Gaskill*) Professor Henry Briggs, Dr. T. Watts Eden and Dr. John Fairbairn all gave evidence and were unable to show that the stated period of gestation was impossible; Professor Briggs had had personal experience of a patient whose pregnancy apparently lasted 306 days, but thought a period of 331 days improbable though not impossible. The legal position then, as in the subsequent cases, was that, in the absence of expert evidence that it was impossible for the husband to be father to the child, the woman could not be found guilty of adultery. It is hard to see that this problem will be readily solved. Even though it may be possible to determine the exact date of conception, as distinct from that of coitus, and to make endless exact measurements of the duration of pregnancy, the exception will still be possible, and one wonders what can stop the period acceptable to a court from increasing by small increments *ad infinitum*.

#### THE TREATMENT OF CARCINOMA OF THE LIP.

CARCINOMA of the lip is responsive to treatment and in its early stages is usually curable. That such an obvious lesion should be left without treatment beyond its early stages is curious but by no means infrequent, and discussion on the most satisfactory form of treatment at all stages still goes on. The setting of X-ray and radium therapy and surgery in opposition would not be approved by many clinicians today; these forms of treatment should be regarded as complementary rather than competitive, as is pointed out by Hayes Martin in an article of a special series published by the American Medical Association in cooperation with the American Cancer Society.<sup>1</sup> Martin's opinion is that for cancer of the lip

surgery alone is preferable in most cases as the primary form of treatment, although supplementary radiation therapy is often indicated should there be postoperative recurrence.

In the treatment of metastasis to cervical lymph glands he considers that

neck dissection is the method of choice in all operable cases. In those situations where cervical metastases are inoperable, or in others where operation cannot be performed because of the presence of an inoperable primary lesion, a program of radiation therapy should be employed. Radiation therapy is often successful in the treatment of inoperable cervical metastatic cancer or in postoperative recurrences.

This general plan of treatment, with an emphasis on surgery, has been substantially followed in the treatment of 407 unselected patients with cancer of the lip at the Pondville Hospital, Walpole, Massachusetts, according to a report by J. E. Cross, E. Guralnick and E. M. Daland.<sup>2</sup> The three-year cure rate was 67.1%. Amongst those patients who received all their treatment at Pondville (242 patients) the three-year cure rate was 81.4%. Many of the others had advanced lesions when they first came to Pondville and some had had unsuitable or inadequate treatment elsewhere. It is emphasized in the report that surgery is the preferred method at the Pondville Hospital and this must be borne in mind in the assessment of the results. The results in the whole group and in the two main subgroups of those treated wholly and those treated partially at Pondville show treatment by irradiation and by combined surgery and irradiation in a most unfavourable light compared with treatment by surgery. It is

pointed out, however, that because of the accepted preference for surgical treatment the radiologists were called upon to treat many lesions which were far advanced and not suitable for surgery. By careful selection comparison was made of treatment by irradiation and by surgery of lesions of comparable size, and the results were much closer, though surgical treatment was still, in general, superior. In the treatment of lesions one centimetre or less in diameter the two methods appeared to be equally effective. Some of the other findings are also of interest. It was found that carcinomata of the labial commissures were approximately twice as difficult to control as lesions in other parts of the lips. The possibility of cure of carcinoma of the lip is directly related to the size and pathological grade of the primary tumour and the presence (or absence) of metastases in lymph glands. Of patients with metastases in cervical lymph glands, proved by pathological examination, who underwent neck dissection, 35.9% attained a three-year cure. Incidentally it was found that in the series as a whole three-year cures were as significant statistically as five-year cures. There are many more details in this Pondville report which might be mentioned, but it is sufficient to remark that it supports the contention that carcinoma of the lip is one of the most readily curable malignant conditions met with in the body. Martin, in the paper mentioned earlier, states that a Gallup poll taken in 1945 revealed that one United States citizen in four thinks that cancer is incurable. Yet he can quote from the Memorial Hospital, New York, a five-year cure rate of 70% amongst all patients with carcinoma of the lip (both early and advanced) and of 86% amongst those with early lesions (primary lesions less than two centimetres in diameter). If patients and doctors can learn to appreciate the possibility of a favourable prognosis, then the early diagnosis and prompt treatment will be made practicable on which in turn the prognosis depends.

#### DERMATOLOGICAL DETECTION.

PERHAPS all diagnosis is a form of detective work, but at least the fondness on the part of detectives, especially those of fiction, to follow the Sherlock Holmes tradition in making use of pieces of obscure medical knowledge justifies the doctor if he wishes to engage in a little detection. A Dundee dermatologist, J. Kinnear, reports a mystery that he encountered.<sup>3</sup> A woman consulted him with recurring blisters on her legs. Across the backs of both calves was a band of erythema studded with bullae up to the size of a pigeon's egg. They were thought to be due to insect bites, but no source of these could be found. A few days later a second woman appeared with exactly similar lesions; but she had observed that they always appeared a few hours after she had been in a tram-car on a certain route. Within a fortnight six women were under observation, all travellers on the same tram route. Inquiry revealed that further female tram travellers were consulting other doctors for similar lesions. At the request of the local medical officer of health, Kinnear inspected a tram-car similar to those used on the route common to the patients. All of the patients travelled on the lower deck where there were two parallel leather-covered seats running from front to rear and kept in place by a vertical slat of wood in front; the lower edge of the slat was at approximately the height of the lesions. Further inspection exonerated all cars but one, in which, lurking in a groove along the lower edge of the slat of wood, were numerous bed bugs. These apparently, in violation of the best bed-bug tradition, slept at night while the car was in the garage and by day sat "in a row along the edge of the wood extracting nourishment from the legs of unsuspecting lady passengers". Men were protected by their trouser legs. Soon the bugs were routed and the epidemic ceased abruptly. Once more it had been shown that crime does not pay, and bed bugs were shown clearly that, no matter how attractive the prospect, they may not aspire to be tram bugs.

<sup>1</sup> The Journal of the American Medical Association, August 7, 1948.

<sup>2</sup> Surgery, Gynecology and Obstetrics, August, 1948.

<sup>3</sup> The Lancet, July 10, 1948.

## Abstracts from Medical Literature.

### THERAPEUTICS.

#### Treatment of Cardio-Vascular Disease.

A. R. BARNES (*The Journal of the American Medical Association*, January 31, 1948) states his views and the views of the Mayo Clinic on the present treatment of heart disease. For congestive heart failure he favours the oral treatment with digitoxin, which he states in full dosage of 1.2 milligrammes causes less nausea and is more fully absorbed than "Lanatoside C" or digitalis leaf. He advises gradual digitalization rather than the full digitalizing dose at the outset in order to avoid toxic effects. In the rare event that urgent digitalization is necessary, he advises the intravenous administration of ouabaine 0.3 gramme, followed by 0.1 milligramme given intravenously every two or three hours if required until a satisfactory result has been obtained. He advocates the use of mercurial diuretics in the treatment of oedema and dyspnoea and refers to the dose of one or two millilitres daily by intramuscular injection recommended by Gold. The author states that the mercurial diuretics will not only remove oedema, but will prevent its development and relieve or prevent dyspnoea. He advises the patient to weigh himself daily, and if he notices a gain of two to four pounds of weight suddenly to report to his physician for an injection of a mercurial diuretic. Under this plan such an injection is found to be necessary from once in two weeks up to three times a week. Patients may accumulate seven or eight pounds of fluid before its presence is indicated by oedema of the dependent portions of the body and by signs of pulmonary congestion. Restriction of salt to 1.5 to 2.0 grammes daily also diminishes the need for mercurial diuretics. The author states that in the treatment of hypertension Kempner has advocated the use of a rice diet and claimed great benefit from such a diet. Grollman has advocated a low intake of sodium (less than 0.5 milligramme daily). For the treatment of subacute bacterial endocarditis doses of 400,000 to 1,000,000 units daily of penicillin were advised for the average subject, but up to 20,000,000 units a day might be necessary for cure. Treatment should be continued for three weeks or more. A failure to obtain a blood culture at that stage indicated that penicillin therapy could be suspended, even though leucocytosis, an increased sedimentation rate and embolic phenomena persisted. Patients with valvular disease who require tooth extraction or tonsillectomy should receive 100,000 units of penicillin every three hours for a day preceding and two days after such surgical procedures as a prophylactic measure. The author states that, in heart failure and acute coronary occlusion, thrombotic or embolic complications occur frequently, and that dicoumarol prevents these accidents and preserves life. He advises the administration of 300 milligrammes of the drug on the first day and with careful prothrombin studies a gradual reduction of dose; daily estimation of the prothrombin level is necessary. If serious bleeding occurs as a result of

the dicoumarol treatment transfusion and intravenous administration of menadione bisulphite are advised. He lists the contraindications to the use of dicoumarol.

#### Digitoxin Intoxication.

A. M. MASTER (*The Journal of the American Medical Association*, June 5, 1948) states that digitoxin poisoning has become a real hazard. Digitoxin, which is an important constituent of "Digitaline Nativelle", "Purodigen", "Crystodigen" and the like, has practically replaced digitalis in America. Gold recommended a single full dose of 1.2 milligrammes of digitoxin followed by 0.2 milligramme for maintenance. This dose has been exceeded frequently, and much poisoning has resulted. The author reports nine cases of digitoxin poisoning, which has the same symptoms and signs as other forms of digitalis poisoning. He records multifocal premature contractions, auricular fibrillation, complete heart block, bradycardia depression of the RST segments of the electrocardiogram, nodal tachycardia, yellow vision, abdominal cramps, diarrhoea, vomiting, psychosis, inverted T waves, prolonged PR interval and sudden death following excessive dosage (over 1.2 milligrammes) or in coronary occlusion. The author concludes that dosage is too haphazard, full doses of 1.2 milligrammes being given to quite small people, regardless of weight. He states that doses given should accord with the patient's weight. Digitoxin is the most cumulative of all digitalis glucosides, and it must be remembered that the daily maintenance dose of digitoxin varies from 0.05 to 0.2 milligramme.

#### Parkinson's Disease.

I. BUDNITZ (*The New England Journal of Medicine*, June 17, 1948) describes the treatment of Parkinson's disease with "Benadryl". Eight patients were treated with 50 milligrammes of "Benadryl" four times daily. Symptomatic improvement was noted. The dose was increased without benefit in some cases, but generally "Benadryl" was given in doses of 50 milligrammes three or four times daily. "Pyribenzamine" was tried in place of "Benadryl" without benefit. In many cases scopolamine 0.6 milligramme given three times daily or one of the other atropine-like drugs was used coincidentally, apparently with benefit, and a synergistic action of "Benadryl" and these drugs is suggested.

#### "Myanesin."

F. M. BERGER AND R. P. SCHWARTZ (*The Journal of the American Medical Association*, June 26, 1948) describe the use of "Myanesin" in spastic and hyperkinetic disorders. They state that "Myanesin" (3-ortho-toloxyl-1,2-propanediol) relaxes spasticity and rigidity. It has been used during anaesthesia in Great Britain. Its action after intravenous administration is evanescent; it is more prolonged on oral administration. It was given by mouth in solution in a dose equivalent to one gramme of "Myanesin" three to five times daily. In the case of hemiplegia and spastic diplegia much freer movement was obtained. In the presence of Parkinson's syndrome tremor and rigidity were relieved. Toxic effects were rare; the drug has been used as described for up to five weeks, but the authors point out that symptoms of poisoning should

be watched for. Anorexia, vomiting, diplopia, nystagmus and muscle incoordination may occur.

#### Neurosyphilis.

L. PARKER CHESNEY AND FRANK W. REYNOLDS (*Archives of Neurology and Psychiatry*, March, 1948) discuss the results of treatment of 54 patients with *tabes dorsalis*; 33 received penicillin alone and 21 had a course of penicillin with malaria. With penicillin alone the symptoms of 27% of patients were relieved and the cerebro-spinal fluid showed a satisfactory response. With combined malaria and penicillin 57% of the patients showed satisfactory improvement. Their results suggest that the combination of malaria and penicillin as a mode of treatment is much superior to penicillin alone. The advantage of penicillin treatment alone lies in its convenience and relative freedom from toxicity.

HENRY EISENBERG AND ALEX S. HERSHFIELD (*The Journal of Nervous and Mental Disease*, July, 1948) describe the use of a new pentavalent arsenical "Aldarsone" combined with bismuth in the treatment of 100 patients with neurosyphilis. No toxic effects were noted. In twelve cases the result of the Eagle Wassermann test became negative and in 58 there was a downward trend in the titre. The authors conclude that the results compare favourably with those from a course of penicillin and fever therapy.

### NEUROLOGY AND PSYCHIATRY.

#### The Chronic Alcoholic.

MOGENS ELLERMANN (*The Journal of Nervous and Mental Disease*, June, 1948) has analysed the history of 231 male chronic alcoholics in Denmark. He concludes that most are constitutional psychopaths. He states that the results of treating in hospital patients with chronic alcoholism are very discouraging. He discusses expensive therapy in mental hospitals and less expensive public temperance institutions, and points out that there must be effective legal means of detention. In his opinion the treatment of choice is to leave alcoholics entirely without any treatment.

L. ERWIN WEXBERG (*The American Journal of Psychiatry*, March, 1948) discusses some aspects of an alcoholic clinic established for some eighteen months. It appears that between 55% and 60% of the 1000 patients treated have received benefit. The clinic is run in close association with Alcoholics Anonymous. The author states that chronic alcoholics frequently show a specific type of emotional attitude. The pattern of behaviour moves from a craving prior to drinking to a dynamic climax terminating in drunkenness, to be followed by a "hangover". Repetition facilitates this compulsive drinking until drinking becomes the climax of ambition, and moral, aesthetic, social or cultural values do not count any longer. This represents the personality change found in alcoholics. Forced abstinence results in an emotional vacuum and sooner or later results in relapse. Active psychotherapy will have to promote restitution of a previously existing range of values. A critical point is reached, when economic disaster is imminent, or earning efficiency is so depleted that another drinking spree



cannot be provided. This is the bankruptcy of the alcoholic personality. At this point suicide or the cessation of drinking are the alternatives. The patient may be receptive for psychotherapy; he has nothing to lose and possibly something to gain. The establishment of a new system of values, recreational and social interests, group therapy with other alcoholics, and the spiritual system of the Alcoholics Anonymous have been used in this clinic.

#### Methyl Hydantoin in Epilepsy.

NORMAN A. DAVID, LLOYD S. DURKIN, MERL L. MARGASON AND WILLIAM A. VIELE (*The Journal of Nervous and Mental Disease*, August, 1948) have treated twenty epileptics with methyl hydantoin. A measles-like dermatitis occurred in three cases. No gum hyperplasia was noted. The authors conclude that the drug is effective in *grand mal* epilepsy and is especially useful in those cases in which phenobarbitone produces mental depression or when diphenylhydantoin sodium is ineffective. It is somewhat more useful than this drug in cases of *petit mal*.

#### Mental Deterioration and Age.

G. A. FOULDS AND J. C. RAVEN (*The Journal of Mental Science*, January, 1948) describe the mental testing of two groups, one of 1047 post office employees and the other of 920 employees of a private firm. The ages varied from seventeen to sixty years. The tests used were Progressive Matrices and the Mill Hill Vocabulary Scale. The authors conclude that the capacity to form comparisons and to reason by analogy slowly declined from the age of twenty-five years, and, if after the age of sixty years the decline continued at the same rate until the age of eighty years, the average person's capacity to grasp new ideas and to adopt new methods would not be greater than that of a child of eight years. The child of this age does not use abstract comparisons and reasoning by analogy as a systematic method of learning. The average ability to recall information reaches its maximum about the twenty-fifth year and remains stationary for the next thirty years. From the age of thirty years the ability to understand new methods of thinking, to adopt new methods of working and even to adjust to new situations steadily decreases. Vocabulary tests are considered to give the best level an individual has attained, whatever his present capacity for intellectual activity may be.

#### Effects of Bladder Distension on Autonomic Mechanisms after Spinal Cord Injuries.

L. GUTTMANN AND D. WHITTERIDGE (*Brain*, December, 1947) discuss the effects of bladder distension on autonomic mechanisms after a spinal cord injury. Their work is based on examination of patients with severe lesions in different parts of the spinal cord. In patients with a complete lesion above the second lumbar segment distension of the bladder is followed by constriction of the blood vessels of the toes. In lesions at or below the sixth thoracic segment this vasoconstriction is accompanied by vasodilatation in the fingers and a slight rise of blood pressure. Where there is a complete lesion at or above the fifth thoracic segment, vasoconstriction of the toes is accom-

panied by vasoconstriction in the fingers and a very large rise in blood pressure. There is also a pronounced decrease in pulse rate and extrasystoles have been noted. Vasodilatation occurs on neck, face and nasal mucosa; this may lead to complete blockage of the nasal airway. Subjectively the patient may complain of different sensations in the chest and severe headache. There is also an increase in sweating; its distribution depends on the site of the spinal lesion. These observations are of importance in emphasizing the role of the autonomic nervous system. They are also important to the patient because by sensations such as increased pulse rate, blushing, or headache he is given information as to the fullness of his bladder.

#### Atypical Intracerebral Haemorrhage.

ERIC C. O. JEWESBURY (*Brain*, September, 1947) discusses atypical types of intracerebral haemorrhage. He considers the significance of arteriosclerosis, congenital aneurysms, vascular anomalies, eclampsia, cerebral tumour, vascular occlusion, *polyarteritis nodosa* and trauma as causes of intracerebral haemorrhage with hematoma formation. After the elimination of these causes there is a group of cases for which no satisfactory explanation is available. Such hematomata are usually superficial, occur in young people, present as slowly expanding intracranial lesions and respond satisfactorily to surgical treatment.

#### Necrosis of the Brain due to Radiation Therapy.

JOB PENNYBACKER AND DOROTHY S. RUSSELL (*Journal of Neurology, Neurosurgery and Psychiatry*, August, 1948) discuss the clinical and pathological features of five cases of necrosis of the brain following radiation therapy. The subjects were treated in different centres with accepted techniques and dosages. In each case there was a long latent period between the radiation treatment and the onset of clinical signs of necrosis. The shortest interval was nine months and the longest five years. The authors state that the clinical effects may come on suddenly or gradually. The pathology is related to necrosis associated with reactions in the smaller blood vessels. As there is no way of telling which patients will develop necrosis, they suggest that radiation should be reserved for cases of inoperable tumours.

#### Motivation in Recovery from Illness.

P. R. HAWLEY (*The American Journal of Psychiatry*, June, 1948) states that the importance of motive in recovery from disease is very great, and he recognizes the absence of the wish to recover or an ambivalent attitude in roughly three types of disability: (i) purely somatic illness for which there is every hope for recovery, (ii) psychosomatic disease, and (iii) devastating incurable physical disability such as blindness or paraplegia. In the first category the disability is used as a retreat, the environment is protective and there is no urge to return to an unpleasant environment. The author found that when soldiers were removed to a rehabilitation centre nine out of ten were bending every energy to recondition themselves. With psychosomatic disease, the tension arising out of

mental conflict needs to be resolved and the patient's resources which have not been adequately utilized require directing into constructive and more satisfying ways, so that greater satisfaction results from doing things rather than in just being. To motivate such a patient successfully his true interests and abilities must be studied and not left to haphazard guessing, which so frequently represents the doctor's interests but has no relation to the patient. As no patient can take an objective view of his own illness, apprehension is unduly aroused by ill-advised comments or an over-cautious attitude on the part of the physician. Familiarity with disease gives the physician some contempt for it, and he discusses it too frankly and too objectively with his patient to whom medical terms are frightening because they are mysterious. With permanent disabilities, attitudes of dependence with fear of being abandoned, feelings of frustration and wishful thinking combine to produce a state of depression in at least 45% of cases. Those who reacted least adversely were usually outgoing and unimaginative and came from stable closely knit family groups. Those who were extremely ambitious or who were emotionally unstable tended to react badly to the devastating disability.

#### Hypoglycaemia.

HAROLD L. MITCHELL, JOHN A. MALCOLM, D. PAUL GREENLEE AND ROBERT C. HAMILTON (*The Journal of Nervous and Mental Disease*, June, 1948) describe a case of islet-cell tumour of the pancreas which did not accord with Whipple's postulates as there was no immediate relief of symptoms after administration of glucose. Notwithstanding this the patient made an excellent recovery after surgical removal of the tumour. The authors point out that reversible changes in hypoglycaemia may come after a surprisingly long period. The patient was in a coma for three days prior to glucose therapy.

MARGARET BASS AND PETER L. GIOVACHINI (*The Journal of Nervous and Mental Disease*, July, 1948) describe a case in which a twenty-eight-years-old housewife had attacks of headaches, sleepiness (most pronounced in the morning) psychotic episodes with hallucinations and a fugitive hemiplegia. A diagnosis of hysteria was made. The fasting blood sugar level was found to be low (30 milligrammes to 18 milligrammes per centum). Finally she made a good recovery after removal of a pancreatic tumour. The authors point out that the organic basis of hypoglycaemia was suggested by the occurrence of the episodes prior to the evening meal, the extreme drowsiness on awaking and the nausea, blurring of vision, clouded sensorium and periods of excitement indicative of a toxic confusional state.

#### General Paresis and Electroplexy.

HARRY C. SOLOMON, AUGUSTUS S. ROSE AND ROBERT E. ARNOT (*The Journal of Nervous and Mental Disease*, April, 1948) have treated 34 general paralytic patients by electroshock and obtained some improvement in 29 cases. They state that the principal use of electroplexy is its quietening effect. The results indicate that the symptoms of the psychoses are not directly motivated by histopathological changes.

## British Medical Association News.

### SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on September 23, 1948, at Sydney Hospital. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staff of the hospital. Parts of this report appeared in the issues of December 11 and 18, 1948.

#### Pulmonary Collapse and Fibrosis.

DR. W. L. CALOV showed a housewife, who had attended first in 1941, at the age of thirty years. She gave a history of having suffered from bronchitis for three years in succession. One week before seeking advice she coughed about one pint of bright blood. She had no cough or sputum or night sweats. Her weight was stationary. For the previous few weeks she had tired easily. No tuberculous contact was known. Her weight was 126 pounds. Her nutrition and physique were good. Scoliosis was noted. The left hemithorax was contracted and its expansion was impaired. The right side expanded well. Bronchial breath sounds were audible in the upper zone of the left hemithorax.

X-ray examination showed dulness and contraction of the left hemithorax, and complete dislocation of heart and mediastinum into it. The trachea and its bifurcation into the right and left main bronchi were noted wide out to the left of the mid-line. Dr. Calov said that, as far as one could see, no change had occurred in these X-ray appearances. The result of the Mantoux test was positive. The erythrocyte sedimentation rate by the micro method was 2.0 millimetres in half an hour and 5.0 millimetres in one hour. The rate had varied from time to time since, but had never been much above normal. Tubercle bacilli had never been recovered from the sputum. From time to time during the years she had coughed a little blood. Her weight had varied from 117 pounds to 140 pounds. At the time of the meeting it was 135 pounds. In 1941 and 1942 the patient had spent four and a half months in a sanatorium.

Dr. Calov said that the clinical findings and the X-ray appearances indicated collapse and fibrosis of a large part of the left lung. This was almost certainly due to bronchial obstruction, and it was probably of many years' duration. The obstruction could have been caused by pyogenic or tuberculous infection. Bronchiectasis was almost certainly present. A rather unsatisfactory bronchogram taken in 1941 showed obstruction to the left upper lobe bronchus and dilatation of several lower lobe bronchi. As the patient was sensitive to iodine, the test had not been repeated.

#### Pulmonary Tuberculosis.

Dr. Calov next showed a sailor, aged fifty-two years, who had reported in May, 1941, with a history of having been discharged from the army fourteen months previously because of tuberculosis. He had been in a sanatorium from April, 1940, to April, 1941. Artificial pneumothorax had been induced, but had been discontinued after eleven months. X-ray examination revealed a huge cavity in the upper zone of the left lung. He attended next in September, 1942, and again in August, 1943. On the last-mentioned occasion he said that he was losing weight and suffering from night sweats. He was noted to have a splendid physique. The left shoulder was flattened somewhat. The expansion of the thorax was good; but the left side lagged slightly. Crepitations were audible in the left axilla and in the left pectoral region. He was admitted to Randwick Auxiliary Hospital.

He did not report again until June, 1945. At X-ray examination in August, 1945, the cavity at the left apex was seen to be smaller. In March, 1946, the cavity could no longer be found. In November, 1946, and on his most recent visit (September, 1948), the X-ray findings were the same as in March, 1946. Until 1943 numerous tubercle bacilli were found whenever the sputum was examined. No record of sputum examination had been made since then.

Dr. Calov said that the patient looked after himself in his own way. For the greater part of 1945 he slept in the Domain for choice and treated himself by taking deep breathing exercises. He lived in the country and seldom came to the city. The only active treatment given to him was artificial pneumothorax for eleven months in 1940-1941. This did him no apparent good. The cavity remained widely open throughout. The patient's X-ray films illustrated the body's natural powers of recovery from the destructive effects of infection with the tubercle bacillus.

#### Pulmonary Neoplasm.

The next patient shown by Dr. Calov was a carpenter, aged forty-nine years, who became troubled with a dry cough at work in February, 1948. The cough persisted. He had no breathlessness, no pain in the chest, and no hæmoptysis. Since February he had lost two stone in weight. In July, 1948, he first noticed swelling of the tip of one of his fingers. The tips of the remaining fingers became affected later. The joints of the fingers and ankles and other joints had become swollen and painful. He had a good physique and his nutrition was satisfactory. Pronounced clubbing of the fingers was present. The interphalangeal joints were swollen. No grossly abnormal clinical signs were to be found on clinical examination of the thorax. X-ray examination revealed a dense shadow in the right hemithorax, limited below by the interlobar pleura.

At bronchoscopic examination on September 21, 1948, Dr. M. P. Susman had found a small, whitish tumour in the trachea and one in the bronchus of the right upper lobe. A piece was removed for biopsy.

#### Broncho-Pleural Fistula.

Dr. Calov finally showed a man, aged twenty-eight years, who had first found that he had tuberculosis in 1941. Artificial pneumothorax of the left side was induced in 1941 and maintained until 1948. Apparently a good deal of fibrosis and collapse was present, as refills were seldom required. He was always lean; but his general condition was fairly good, and it was thought that the disease was under fairly good control.

In January, 1948, he had what he regarded as an attack of influenza and became breathless. He was admitted to hospital on January 27, 1948. At that time he was very ill. He had a high fever and a rapid pulse. Signs of hydropneumothorax were present on the left side. Splashing sounds, cavernous breath sounds and consonant râles were audible. The patient volunteered the information that when he turned in a certain way and coughed, he spat up large quantities of thin sputum. He could feel the fluid splashing in his chest. X-ray examination revealed a fluid level high in the left hemithorax and evidence of a recent bronchogenic spread of tuberculosis in the right lung. He was given streptomycin in a dose of 2.0 grammes daily.

A pneumothorax needle was inserted high in the left pleural cavity, and a reading of *plus* and *minus* atmospheric pressure was obtained. This suggested that the pleural cavity communicated with the atmosphere by way of a broncho-pleural fistula. Thin murky fluid was aspirated. At the end of the aspiration the manometer reading was unchanged.

Aspiration was repeated from time to time. The patient knew when aspiration was due, because as the hemithorax filled with fluid he would begin to spit it out. At each aspiration streptomycin was injected into the pleural cavity. In the course of time the fever subsided and the patient's weight began to increase. A total of 60 grammes of streptomycin was given.

Surgical assistance was required. On April 6, 1948, Dr. M. P. Susman performed the first stage of a thoracoplasty. The third and final stage was carried out on May 25.

Dr. Calov said that the patient was now able to walk about. He felt fairly well, but was weary of a hospital existence. He was ready for sanatorium. He still had his broncho-pleural fistula. The condition of the right lung was much better.

## Medical Societies.

### THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held on June 6, 1947, at the Institute of Medical and Veterinary Science, Adelaide.

#### Factors Influencing Skin and Hair Colour.

A discussion took place on factors influencing the colour of the skin and hair.

#### Permanent Waving.

PROFESSOR J. B. CLELAND called attention to the summary given in *Nature* of January 25, 1947, at page 115, of an article by R. E. Billingham and P. B. Medawar under the



title of "The 'Cytogenetics' of Black and White Guinea-Pig Skin". The summary was as follows:

Black guinea-pig epidermis has the power to "infect" neighbouring white epidermis, and so to blacken it. This is shown not to be due to a cellular invasion and a replacement of white cells by black. It is due to an agent which, having entered white cells, brings about a permanent heritable change that causes them and their descendants to remain thereafter black. The infective agent may be a self-reproducing body housed normally in the cytoplasm; or, less probably, it may be morphogenetic hormone that merely initiates the formation of such self-reproducing bodies in the white cells which it infects. The experiments described have a direct bearing on the problems of somatic cellular differentiation and heredity.

Professor Cleland also showed samples of hair of a woman, aged between forty-seven and fifty years, with fair hair becoming slightly grey. A month or so previously she had had her hair permanently waved by a hairdresser. On removal of the apparatus from her head, the hair treated was found to have become a darker brown, to the dismay of the hairdresser and the consternation of the subject. The method of permanent waving in that case was non-electric. The hair was first wet with *Liquor Ammonia Fortis*, sodium sulphite, some Turkey red oil, glycerin, methylated spirits and distilled water. These were applied to the distal part of the hair. Sodium sulphite replaced sodium sulphate for application to the base of the hairs. Clips were then applied, electrically heated, which fell off in ten to fifteen minutes. Probably the same method of permanent waving had been applied on a previous occasion, about November, 1946, by another person in the same establishment, without any alteration in colour. Other women with hair as light had had their hair permanently waved about the same time with no change in colour. Customers were always asked if the hair had received any treatment previously. In this case no information of the recent application of any substance to the hair was obtained. The hairdresser, in supplying the information, stated that he had known darkening of the hair to occur in women taking tonics, especially after confinements. A band up to an inch or more of darker hair might be produced. Professor Cleland said that it would be interesting to know if the tonics contained iron or small quantities of copper.

#### *The Relationship of Copper to Pigmentation in Black-Woolled Sheep.*

Mr. H. J. LEE said that the many and various breeds of sheep differed greatly in their genetical propensity for laying down pigment in the skin and keratinous outgrowths such as wool, horns and hoofs. Some so-called English black-faced breeds invariably laid down melanin in the short hair covering the face, the ears and the extremities of the limbs, as well as in a proportion of the wool fibres of the body coat. In other breeds the majority of the members of which normally produced no melanin, occasional individuals possessed the inherent capability of producing that pigment. Some observations had been made elsewhere (by Dr. R. B. Kelly) on genetical aspects of that phenomenon as it occurred in merino sheep; but they would not be discussed.

In such sheep the pigmented areas might be restricted to one or more isolated small spots, or might involve the whole surface of the sheep. The regions of the skin from which pigmented wool fibres grew always appeared pigmented, whereas unpigmented fibres grew from regions free from pigment.

In some areas throughout Australia there had been observed from time to time a phenomenon commonly known as "banding" in the wool of sheep genetically constituted to produce pigmented fibres. It was due to the intermittent loss, partial or complete, of pigment from restricted regions of the staple. Periods of wool growth of variable duration, during which pigment was relatively lacking, alternated with periods during which pigmentation was partially or completely restored.

The role of copper in normal melanin formation was well established, and observations strongly suggested that that relationship applied in sheep as well as in other animals. A strong correlation had been observed in some parts of Australia, where surveys had been attempted, between the occurrence of banding and other manifestations of copper deficiency in sheep such as the loss of normal crimp, which was known in South Australia as "steeliness". When black-woolled sheep were confined to copper-deficient pastures, commonly both crimp and pigment disappeared from the wool fibres produced, and both might be restored simultaneously by appropriate copper therapy. However, in

many naturally occurring instances, pigment might disappear without loss of crimp. This suggested that if loss of pigmentation in the field was always associated with an insufficient supply of copper, the system responsible for pigmentation might be more sensitive to copper deprivation than was the mechanism of crimp formation. If that could be proved unequivocally, then banding in black wool might prove to be a useful early indicator of copper deficiency affecting sheep in the field.

Histological studies relevant to those observations had been made by Mr. H. B. Carter in Sydney, who had first drawn attention to the concurrent disappearance of crimp and pigment from some naturally occurring banded wools. In experimental copper-deficient black sheep pigmentation had been restored by the administration of copper by mouth or by intravenous or subcutaneous injection. It was interesting to note that they had not experimentally succeeded in restoring pigment in the narrow, sharp bands which frequently occurred naturally, but they were attempting to do so by supplementing the diet of sheep with suboptimal doses of copper. That procedure might raise the peaks of the normal seasonal fluctuations of blood copper levels to a point adequate for complete pigmentation until the blood copper level dropped once more.

In none of their copper-deficient black sheep had pigmentation been observed to fall in the hair of the face, ears or lower limbs, or in the horns or hoofs. That was possibly related to the comparatively slow rate of growth of those structures.

Mr. Quinlan-Watson, of the Division of Biochemistry, hoped to establish the relationship of copper to pigmentation in sheep by studying manometrically the dopa enzyme activity of skin preparations from pigmented and unpigmented areas in normal and copper-deficient sheep. Unfortunately dopa was not readily available, and they would be most grateful if anybody could provide a small quantity for that purpose.

#### *Black Hair in a Fawn Rabbit.*

Mr. F. DRAPER described the temporary production of black hair in a fawn rabbit, from an area where necrosis had been induced by injection of toxin from a virulent strain of *Staphylococcus aureus*. The site of injection had previously grown fawn-coloured hair, but after the necrosis had healed a black streak of hair appeared there. Some time later the black hair was replaced by hair of the original fawn colour.

## Post-Graduate Work.

### THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

#### PROGRAMME FOR 1949.

THE Post-Graduate Committee in Medicine in the University of Sydney announces the following programme of courses for 1949. Except for those shown during the months January-March, all dates are tentative only, depending on the number of candidates offering and subject to confirmation. Intending candidates are advised to make early application to the Course Secretary, the Post-Graduate Committee in Medicine, 131, Macquarie Street, Sydney, as soon as possible. Telephones: BU 5238, BW 7483. Telegraphic address: "Postgrad, Sydney."

#### Course in Haematology.

Professor L. S. P. Davidson, B.A., M.D., F.R.C.P., Professor of Medicine in the University of Edinburgh, will conduct a short course of lectures in haematology beginning on February 14, 1949, the complete programme of which will be announced shortly. Fee for attendance will be £3 3s., and those interested in attending are requested to notify the Secretary as soon as possible.

#### General Revision Course.

The general revision course, devoted mainly to problems of therapy, will be conducted in Sydney for two weeks beginning May 23, 1949.

#### Anæsthesia.

A course suitable for candidates for the diploma in anæsthesia will begin on June 6, 1949, for six months, consisting of lectures, demonstrations *et cetera*, held mainly during the afternoons.

**Dermatology.**

A course for part I of the diploma in dermatology will be held in the afternoons for three months beginning June 20, 1949. This will be followed on September 19, 1949, by a part II course of approximately six months' duration. It is probable that more preclinical work will be required and intending candidates are advised to commence their studies and attendance at hospital clinics as early as possible. Further details may be obtained on application to the Course Secretary.

**Gynaecology and Obstetrics.**

A part I course for the diploma in gynaecology and obstetrics will begin for approximately ten weeks on August 29, 1949, all sessions being held in the afternoons. A part II diploma course will begin on January 10, 1949, for twelve weeks. In addition, it is hoped that a full-time course of an advanced nature suitable for general practitioners will be held for two weeks during August-September.

Short post-graduate residencies may be arranged at the Women's Hospital, Crown Street, for which due notice is required.

**Laryngology and Otorhinology.**

Part-time courses for parts II and I of the diploma in laryngology and otorhinology will begin on January 10, 1949 (twelve weeks), and August 29, 1949 (ten weeks), respectively.

**Medicine.**

Two part-time courses in advanced medicine suitable for M.R.A.C.P. candidates will be conducted for fifteen weeks each beginning January 3, 1949, and June 6, 1949.

**Medical Statistics.**

On the second Wednesday of each month seminars in medical statistics are held at 5.45 p.m., usually at the School of Public Health and Tropical Medicine, University Grounds. The subject of each seminar is announced monthly.

**Ophthalmology.**

A part-time course for part I of the diploma in ophthalmology will begin on August 29, 1949, for twelve weeks. A course for part II will begin on January 10, 1949, for twelve weeks.

**Clinical Pathology.**

A course for the diploma in clinical pathology will begin for approximately six months on July 11, 1949, consisting of lectures on three days each week.

**Psychological Medicine.**

A part I course for the diploma in psychological medicine will begin on March 21, 1949, for approximately nine months. A part II course will not begin before late March.

**Radiology.**

A course for the diploma in diagnostic radiology will begin on March 21, 1949, for twelve months. This course requires full-time attendance throughout the entire period, and arrangements are made for post-graduates to be allocated to the radiological departments of hospitals recognized for the diploma for practical work over this period.

**Surgery.**

A course for part II of the degree of master of surgery will begin on January 10, 1949, for twelve weeks and will be followed by a part I course on August 29, 1949, for approximately twelve weeks.

The Post-Graduate Committee reserves the right to limit the number of enrolments in any course.

Copies of the By-Laws and Regulations of the University of Sydney governing any of the above degrees or diplomas may be obtained on application to the office. Examinations are usually conducted once each year in April or May and application must be made to the Dean of the Faculty of Medicine concerning eligibility.

**Individual Post-Graduate Clinical Study.**

Attendance at general or special clinics can be arranged with due notice to meet individual needs.

**Country Courses.**

To date, the following dates have been arranged for week-end courses to be held at the following centres: Armidale, March 5-8; Albury, May 7-8; Katoomba, May 21-22; Broken Hill, June 11-12; Lismore, August 6-7; Kempsey, August 13-14; Parramatta, October 15-16; Newcastle, October 29-30.

**FILM LIBRARY.**

Films may be borrowed by various authorized bodies from the library of the committee upon application to the Secretary. A loose-leaf film catalogue is now available, containing appraisals, the fee for which is £1 ls.

**VISUAL AIDS DEPARTMENT.**

The visual aids department of the Post-Graduate Committee can supply strip films, lantern and other slides. All inquiries concerning this work should be addressed to the Secretary.

**Correspondence.****REITER'S DISEASE.**

SIR: We have read with great interest the paper on Reiter's disease presented in the issue of November 20, 1948 (page 600). The case described is no doubt one of Reiter's disease, but does not illustrate two interesting and characteristic physical signs—namely, those affecting the eye and the throat. In the last six months we have seen two patients with this disease, one in the convalescent stage, and one from the onset whom we treated in hospital. We agree that neither sulphonamides nor penicillin has much effect on the course; but in the one case in which we gave treatment we were much struck with the effect of artificial fever, although it must be admitted that the course of the latter could have been intensified.

As we did not observe the clinical course of the disease in the first case, it may be summarized briefly. The onset was in Japan; the patient first came under observation because of non-specific urethritis, which ran a long course in spite of routine treatment with sulphonamides and penicillin. Later the right knee became swollen and painful, and subsequently conjunctivitis appeared in the left eye. Gonococci were never demonstrated in the urethral discharge, although the patient admitted intercourse some seven days prior to the onset of the urethritis. The result of the gonococcal complement fixation test was negative. The interesting point about this case was that there were two recurrences of the "arthritis" of the knee (X-ray examination subsequently revealed mild osteoarthritic changes) and three recurrences of the conjunctivitis. The cornea had become extremely sensitive to injury, and a slight amount of dust or bright sunlight would cause inflammation.

The second case history is as follows. J.M., a male patient, aged nineteen years, was admitted to hospital on September 17, 1948, complaining of a urethral discharge of three days' duration with slight scalding on micturition. He denied ever having had sexual intercourse, a statement which we had every reason to believe. The discharge was thin and yellow. Physical examination revealed no other abnormalities.

Examination of a urethral smear taken on the patient's admission to hospital revealed numerous pus cells and a few epithelial cells. Treatment was commenced with the administration of sulphathiazole, an alkaline mixture and increased fluids. On September 21 the position was unchanged; the urine was very "dirty", and on microscopic examination of a centrifuged specimen numerous pus cells only were found. The administration of sulphathiazole was continued, and "Mapharsen" (0.06 gramme) was given intravenously. Three days later there was some diminution of the urethral discharge, but some warty lesions had begun to develop on the *glans penis* and just behind the corona. These were treated by the local application of *Liquor Epispasticus* without much effect, and 300,000 units of penicillin in oil were given.

On September 25 the patient complained of malaise and of pain in the region of the sternal angle; he was flushed, and generalized erythema of the trunk and generalized enlargement of the lymph nodes were present. His temperature was normal, but several eroded patches 0.5 centimetre in diameter were seen at the junction of the hard and soft palates. As he had received 36 grammes of sulphathiazole up to that time, it was thought that he was suffering from overdosage, and the administration of the drug was stopped. The leucocytes numbered 12,000 per cubic millimetre, 62% being polymorphonuclear cells. On the following day linitis was present in both eyes. The erythema had faded in three days, although the pain in the chest and the linitis remained unchanged. Culture from the urethral discharge yielded a scanty growth of staphylococci only. The administration of penicillin in water was then commenced, but no change had occurred after 250,000 units had been given—the



urethral discharge continued unabated. On October 5 a course of "Albucid" was commenced, and on the following day the transverse tarsal joint of the right foot became swollen and painful, although there was no pyrexia. On the following day it was decided to commence artificial fever therapy (with the intravenous injection of "T.A.B."), as pain was present in the lower thoracic region of the spine. The result was striking; considerable relief of the urethritis and the joint lesions occurred; the left eye cleared, but the right deteriorated with some corneal ulceration. On October 13, six days later, artificial fever treatment was repeated, with the same improvement, this time in the right eye and the palate lesions, which continued to mend slowly; the joint pains had completely disappeared by October 19. However, the urethral discharge and the penile lesions were still present, and by this time there was considerable excretion of the external urinary meatus. This gradually cleared, and the patient was sent on sick leave on November 5. His condition on review on November 19 (after fourteen days) was satisfactory; both eyes were clear, and there were no joint pains or objective signs of arthritis. Urethroscopy revealed one inflamed Littre's gland, which was cauterized.

When the triad of signs characteristic of Reiter's disease appeared, in view of the negative findings with regard to urethritis and the negative response to the gonococcal complement fixation test, the diagnosis seemed assured, and there seems no reason to change it. It was argued at the time that "Albucid" had a beneficial effect; but no recovery, rather general deterioration, took place until immediately after the first bout of artificial fever. The points of interest in this case are the persistence of the iritis and the erosions of the palate; both these lesions were treated on general lines and were slow to resolve. Our conviction is that as soon as the diagnosis of Reiter's disease is established, artificial fever therapy should be tried as a routine measure, in view of the benefit described in former cases.

Another point which arises is that this condition is not so rare as has been formerly supposed. Cases are no doubt missed because of the mildness of the joint and eye lesions, or, as Osmond<sup>(1)</sup> remarks, because of the clinical similarity to "non-specific urethritis" or gonorrhoea. The joint changes and irritable eye in the first case lead colour to the observations of Vallee,<sup>(2)</sup> who states that permanent eye and joint lesions may occur.

Yours, etc.,

Royal Australian Air Force,  
Laverton,  
November 23, 1948.

C. LELEU.  
C. MCCANN.

#### Reference.

<sup>(1)</sup> T. E. Osmond: *Bulletin of Hygiene*, Volume XXI, 1946, page 739.

<sup>(2)</sup> B. L. Vallee: "Reiter's Disease: Review of the Literature, with Presentation of a Case", *Archives of Internal Medicine*, Volume LXXVII, 1946, page 306.

#### EMPIRE MEDICAL ADVISORY BUREAU.

SIR: The Empire Medical Advisory Bureau has been established by the Council of the British Medical Association with a view to welcoming and providing a personal advisory service to practitioners visiting the United Kingdom, particularly those from the Dominions and Colonies. The Bureau was officially opened by Lord Addison (Lord Privy Seal) on July 13, 1948, at a reception given by the President and Council of the British Medical Association at British Medical Association House, and since then the use made of the Bureau has shown a gratifying and steady increase.

In the first three months some three hundred overseas doctors have made either written inquiries or personal visits. Just over half of their queries have concerned the various aspects of post-graduate education, whilst one-quarter deal with the difficult problem of finding somewhere to live. General inquiries make up nearly one-fifth of the total and cover a wide field, for example, from advice on the inoculation of infants to information on petrol rationing in European countries.

In those cases where doctors have let us know of their impending arrival, the port health officers have been glad to meet and welcome our friends and pass on any urgent messages re accommodation.

We have made a start at arranging social functions at which the visitors have an opportunity to meet members of the profession in this country, and in spite of evening lectures and clinics, nearly 200 overseas doctors and wives have been able to attend these to date.

Our modest activities to date are but an earnest of our intention to make our overseas visitors feel at home as soon as possible in this country.

It will enable the Bureau to be of most service if a visitor gives as long notice as possible of his intended visit to this country and information on the following lines would be useful: projected date of arrival, mode of travel, whether accompanied by wife, period of stay, main and other objects of visit and requirements from the Bureau. A letter of introduction from the local honorary secretary of the visitor's medical association, whilst not essential, would be welcome.

All letters should be sent to me at the undermentioned address.

Yours, etc.,

H. A. SANDIFORD,  
Medical Director.

Empire Medical Advisory Bureau,  
British Medical Association House,  
Tavistock Square,  
London, W.C.1.  
November 26, 1948.

#### SPIRITS AS A DISINFECTANT.

SIR: It is trite and astonishing that in 1948 methylated spirit is still used in many quarters, medical and hospital, as a disinfectant for surgical ware, especially syringes. In spite of frequent demonstrations that methylated or rectified spirits; pure or dilute, will not kill spores, some of us still rely upon them. It is high time that this practice was interdicted. Striking proof of the necessity of this is given us in the recent demonstration of live organisms in museum specimens preserved for a generation in spirit. We owe a duty to our nurses to see that spirit is banned in these regards in all hospitals.

Yours, etc.,

"LISTER."

Brisbane.

December 2, 1948.

#### A NATIONAL HEALTH SERVICE

SIR: We are writing as three of the younger members present at the meeting of the New South Wales Branch on Friday, November 26. From personal experience of a Commonwealth department, we know how repressive and enervating is departmental control.

We congratulate the members present on their unanimous firm attitude, but feel that, in reality, little was achieved. What we ask is a positive statement from the Federal Council of the British Medical Association, with the greatest possible publicity, of what it considers is required to improve medical services, especially to the group known as the "middle class". We consider that negotiation with this present Government or any other political party is undesirable and dangerous. A perusal of Winston Churchill's "Memoirs" will show the real dangers of appeasement by negotiation on principles, even such as those adopted by the meeting. We also feel that our point of view is not well appreciated by senior members of the profession who will be relatively unaffected by the introduction of a general medical service.

We suggest that the public statement (which, of course, would be submitted to the Branches previously) is an urgent matter as the public will not be solidly behind a continued negative policy. It should, in our opinion, take the form of three separate entities.

1. That the profession agrees that society as a whole, rather than the individual, should meet medical costs by some form of insurance on a contributory basis, preferably by an extension of the existing medical benefits scheme, but, failing that, by the patient presenting the doctor's receipt and being reimbursed by the State.

2. That the portion of social services tax collected for medical purposes be used for building and rebuilding hospitals, raising nursing and domestic staffs' salaries to obtain the required numbers, providing sanatoria, mass chest radiography, mental, chronic and convalescent hospitals, research, anti-venereal disease measures and campaigning, and all the rest of the urgently required measures. That it is a retrograde step to spend money on a general medical service till the above matters are put in order, and that, further, no such service would be in the public interest, introducing all the evils of governmental control.

3. That the British Medical Association will set about creating a better medical service of its own devising. We suggest that group practice with local specialists in the group (general practitioners with special interests) is the ideal, these to be self-governing with a special committee of the association to give advice and settle disputes in each



Branch. That groups be practically universal and thus bring about decentralization of specialist and hospital services; those who have seen Nagasaki and Hiroshima have lost interest in great "medical centres" in the middle of cities!

This may sound idealistic, it may seem that a number would have to make great sacrifices, but is it not better to sacrifice the fringes of individual liberty for the community good (and the more civilized the person, the more he recognizes the limits of his "freedom" in relation to society as a whole) than to sell our very souls to a system we know will eventually blind them in chains? Cooperation and friendly help amongst the profession, one to another, will achieve much; otherwise we will negotiate a series of "Munichs" and find there is no power left with which to fight at the end.

Yours, etc.,  
F. C. ARCHIBALD,  
ROBERT GREEN,  
W. VAN GELDEREN.

Sydney,  
December 1, 1948.

## Research.

### ELBERFELD CARD INDEX OF CHEMICALS.

A COPY of the Elberfeld card index of chemicals, consisting of 3000 cards, has been sent to Australia by the Australian Scientific Technical Mission in London. It gives the chemical and physical properties, technical uses and, in particular, physiological effects on humans and animals of a wide range of chemicals prepared and tested by I. G. Farbenindustrie, Elberfeld. This information should be of particular value to workers in toxicology and industrial hygiene.

The index has been passed by the Division of Industrial Development to the Defence Research Laboratories, Maribyrnong. As part of their service to secondary industry, the Defence Research Laboratories will make the information in this index available to interested persons. Inquirers may visit the Defence Research Laboratories and use the index for themselves or send or telephone their inquiries to the Defence Research Laboratories Technical Information Section, Private Bag Number 4, Post Office, Ascot Vale, W.2 (FU 022, extension 1047).

## Nominations and Elections.

THE undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Smith, Mervyn Keith, M.B., B.S., 1944 (Univ. Adelaide),  
29, Fisher Street, Fullarton, South Australia.  
Fisk, Graham Bristow, M.B., B.S., 1946 (Univ. Adelaide),  
130 A.G.H., Kure, Japan.

The undermentioned has applied for election as a member of the Tasmanian Branch of the British Medical Association:

Vaughan, John Vincent, M.B., B.S., 1944 (Univ. Melbourne), Devonport, Tasmania.

## Medical Prizes.

### NAPT PRIZE FOR ESSAY ON COLONIAL TUBERCULOSIS.

A PRIZE of one hundred guineas will be awarded by the Council of the National Association for the Prevention of Tuberculosis for an essay on "The Control of Tuberculosis in a British Colony". The competition is open to doctors of either sex who are in the service of colonial governments, and who are of not more than ten years' or less than five years' medical standing, of which at least three years have been spent overseas in a medical capacity.

Competitors should describe their own proposals for a practical scheme for the clinical, social and administrative control of tuberculosis, either in the British colonies as a whole, or in one or more of them separately. Writers should give their own opinions based on personal experience of public health and anti-tuberculosis work.

Essays should be sent to Dr. Harley Williams, Secretary-General, National Association for the Prevention of Tuberculosis,

Tavistock House North, Tavistock Square, London, W.C.1, to arrive not later than May 1, 1949. The award of the prize will be notified at the NAPT Commonwealth and Empire Health and Tuberculosis Conference in London in July, 1949. Essays sent in shall become the property of the NAPT, and any of them may be published at its discretion in the author's name.

## Diary for the Month.

JAN. 5.—Western Australian Branch, B.M.A.: Council Meeting.  
JAN. 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.  
JAN. 11.—New South Wales Branch, B.M.A.: Council Quarterly.  
JAN. 13.—South Australian Branch, B.M.A.: Council Meeting.  
JAN. 13.—Victorian Branch, B.M.A.: Organization Subcommittee.  
JAN. 14.—Queensland Branch, B.M.A.: Council Meeting.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

**New South Wales Branch** (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phoenix Mutual Provident Society.

**Victorian Branch** (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

**Queensland Branch** (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

**South Australian Branch** (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

**Western Australian Branch** (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

## Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognise any claim arising out of non-receipt of journals unless such notification is received within one month.

**SUBSCRIPTION RATES.**—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and book-sellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £2 per annum within Australia, payable in advance. The rates for subscribers outside Australia may be obtained by applying to the Manager.

# THE MEDICAL JOURNAL OF AUSTRALIA



VOL. II.—35TH YEAR.

SYDNEY, SATURDAY, DECEMBER 25, 1948.

No. 26.

**COMMONWEALTH OF AUSTRALIA.****DEPARTMENT OF HEALTH.****PENICILLIN**

Commonwealth Penicillin is available in the following packs:

1 bottle containing	100,000 units; also in boxes of 5 bottles.
1 " "	200,000 " " " " " 5 "
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**OILY INJECTION OF PENICILLIN**

2 mil. ampoule,	125,000 units per mil.
1 10 mil. bottle,	125,000 " " "
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1 10 mil. bottle,	300,000 " " "

**PENICILLIN OINTMENT, B.P., 500 units per gramme.**

Tube containing 30 grammes.

**PENICILLIN OINTMENT FOR THE EYE, B.P., 1,000 units per gramme.**

Tube containing 4 grammes.

**PENICILLIN CREAM, B.P.**

Penicillin Cream B.P. is available in packets holding—

- 1 ampoule containing 7,500 units of Penicillin;
- 1 ampoule containing Sterile Distilled Water;
- jar containing sufficient base to make  $\frac{1}{2}$  oz. of Penicillin Cream, B.P.

**STERILIZED PENICILLIN CREAM, B.P.**

Sterilized Penicillin Cream, B.P., is available in packets holding—

- 1 ampoule containing 7,500 units of Penicillin,
- Sterile Distilled Water,
- $\frac{1}{2}$  oz. jar of cream base.

**PENICILLIN LOZENGES, B.P., 500 units per lozenge.**

Bottles containing 25 lozenges; 50 lozenges; 100 lozenges.

**PENICILLIN SULPHANILAMIDE POWDER, 5,000 units Penicillin per gramme.**

Bottle containing 10 grammes.

**STERILE DISTILLED WATER****Sterile Saline**

Specially prepared for use with Penicillin.

10 c.c. ampoule; 5 x 10 c.c. ampoules; 12 x 10 c.c. ampoules.

**PRICES ON APPLICATION**

Supplies of these products are available direct from the Commonwealth Serum Laboratories, and also from the undermentioned Senior Commonwealth Medical Officers:

**NEW SOUTH WALES:** Erskine House, 39 York Street,

Sydney.

**VICTORIA:** 113 Queen Street, Melbourne.**QUEENSLAND:** Anzac Square, Adelaide St., Brisbane.**SOUTH AUSTRALIA:** C.M.L. Building, 41-47 King

William Street, Adelaide.

**WESTERN AUSTRALIA:** 4th Floor, G.P.O., Perth.**TASMANIA:** Howick Street, Launceston.**COMMONWEALTH SERUM LABORATORIES**

Parkville, N.2, Victoria, Australia



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**ROYAL PRINCE ALFRED HOSPITAL, CAMPERDOWN, N.S.W., FAIRFAX INSTITUTE OF PATHOLOGY.**—Applications are invited from qualified medical graduates for the position of Vocational Fellow in Pathology at a salary of £490 per annum (subject to basic wage variations) plus board and residence. The appointment is in the first instance for one year, and, subject to satisfactory service, for reappointment for a second year. Successful applicant will commence duties in January, 1949. Fellow will receive training in all branches of pathology, together with an opportunity for studying for the University Diploma in Pathology. Applications in writing close with the undersigned on Friday, 31st December, 1948.—H. SELLE, General Superintendent.

**WANTED, rooms in Macquarie Street, Sydney, for ophthalmic practice, share or full time, mornings essential. Prepared to buy in established practice. Meanwhile available for locum tenens or work during morning. Dr. H. C. BECKETT, 63 Darling Point Road, Darling Point, FB 1801.**

**BRISBANE AND SOUTH COAST HOSPITALS BOARD.**—Applications are invited for a Full-time Medical Officer in the Pathology Department, Brisbane Hospital. Salary range: £1,007 to £1,257, plus board and quarters, or a living-out allowance of £100 in lieu thereof. Commencing salary will depend on experience. The present medical staff of the laboratory consists of two part-time directors and one junior resident medical officer. Applicants must state age and experience. Particulars may be obtained from the General Superintendent, Brisbane Hospital. Applications should be addressed to the Manager, Brisbane and South Coast Hospitals Board, Herston Road, on or before 31st December, 1948.

## ROYAL AUSTRALIAN AIR FORCE: VACANCIES FOR MEDICAL OFFICERS.

**Duties.**—These involve medical duties including active clinical work and the study and practice of aviation medicine at service hospitals and R.A.A.F. units throughout Australia and abroad. Successful applicants will be given the opportunity to continue their studies for higher degrees at training hospitals and universities.

**Qualifications Required.**—Applicants must be British subjects and legally qualified medical practitioners, and must be physically fit.

**Conditions of Service.**—Successful applicants will be appointed to short service commissions of two or four years' duration, and extensions of one year up to a maximum of three years may be granted. A proportion of those so appointed will be granted permanent commissions.

Appointments will be made to the rank of Flight Lieutenant in the first instance, and a gratuity of £250 or £500 is payable on completion of a two or four year short service commission.

Rates of pay applicable per day are shown below:

	Single Officers.		Married Officers.		
	Living on Station.	Living off Station.	Living on Station in Married Quarters or at Home.	Living on Station in Single Quarters.	Living off Station and away from Home.
Basic pay	30/-	30/-	30/-	30/-	30/-
Allowances—					
Special	12/-	12/-	12/-	12/-	12/-
Uniform	1/-	1/-	1/-	1/-	1/-
Marriage	—	—	4/-	4/-	4/-
Provision	—	—	4/-	—	—
Separation	—	—	—	3/-	3/-
Living out	—	5/6	—	—	7/-
	43/-	48/6	51/-	50/-	57/-

Successful applicants will receive free initial issue of clothing and necessaries. Full information and conditions of service available on application to the Secretary, Department of Air, Victoria Barracks, Melbourne.

**APPLICATIONS** are invited from fully qualified medical practitioners for the position of Part-time Medical Superintendent, Taroom Hospital, Queensland, with salary range £560 to £710 per annum, together with the right of private practice, and £109 per annum plus car mileage for attending out-patient centre at Wandooan. Four weeks' annual leave granted on full pay. Partly furnished residence is available with electric light and water supplied. Applications to be in the hands of the Secretary, Hospitals Board, Taroom, Queensland, by noon on January 8, 1949. Applicants to state the earliest duties can be commenced.

## WESTERN AUSTRALIA

Practices for sale, locums supplied, partnerships arranged. Details supplied by air on application. Ships' surgeons, holiday trip to Singapore.

**NEILSON HANCOCK,**

205 St. George's Terrace, Perth  
Telegraphic or Cable Address:  
"Westgraph, Perth."

**BLACKALL HOSPITALS BOARD.**—Applications are invited from persons holding qualifications prescribed by "Hospital Acts, 1936 to 1944", Queensland, for appointment to position of Medical Officer, Isisford Hospital, Isisford. Salary rate £710 per annum. Appointee to have right of private practice (unopposed). Private rooms available at hospital for private patients. Partly furnished residence together with fuel and lighting are provided free by the Board. Applicant to forward qualifications and experience to the secretary of the above Board. Position becomes vacant in January, 1949.

## TASMANIA: DEPARTMENT OF PUBLIC HEALTH.

### GOVERNMENT MEDICAL SERVICES.

Applications are invited from qualified medical practitioners for the following appointments:

- (1) Medical Officer, Hydro-Electric Construction Works, Butler's Gorge, Bronte. Salary: £1,250 per annum. Residence available.
- (2) Two positions for Government Medical Officers in country districts. Salary: £1,000 per annum.
- (3) Two positions for Relieving Government Medical Officers. Salary: £1,000 per annum plus 10s. per day travelling allowance.

For the positions under (2) and (3) other conditions of employment provide for (a) limited private fees for out-of-hours consultations; (b) the payment of 8d. per mile up to 4,800 miles and 7d. per mile for any subsequent mileage in any one year for use of own motor-car; (c) three weeks' annual holiday leave on full pay; (d) sick leave in accordance with a prescribed scale.

Approved travelling expenses incurred on first appointment are refunded after six months' service.

Applications, stating age, experience and marital status, and accompanied by copies of recent testimonials, should be addressed to the undersigned.

F. A. DRISCOLL,  
Secretary for Public Health.

## THE WOMEN'S HOSPITAL (CROWN STREET): JUNIOR RESIDENT MEDICAL OFFICER.

Applications are invited, closing date 15th January, 1949, for one Junior Resident Medical Officer. Duties to commence 1st February, 1949. Remuneration at the rate of £325 p.a. plus board and residence. Apply Secretary.

## MEDICAL SUPERINTENDENT.

Applications are invited from qualified medical practitioners for the position of Medical Superintendent at Base Hospital, Cloncurry, Queensland. Applicant should state whether he desires appointment in a full-time capacity or on a part-time basis, with the right of private practice. The conditions attached to appointment are as follows: (a) Full-time appointment: Salary range £1,094 to £1,344, plus sustenance allowance of £75 per annum. Salary in excess of the minimum may be paid according to qualifications and experience. Salary is also subject to any further basic wage adjustments. Partly furnished residence provided and free fuel and light supplied. Annual leave of four (4) weeks on full pay. (b) Part-time appointment with right of private practice: Salary range £510 to £660. Actual salary will be determined having regard to the amount of service rendered. Residence is available at a reasonable rental. There is no doctor in private practice in Cloncurry. Three months' notice will be required on either side to terminate appointment. Daily average in-patients twenty-two (22) and out-patients fifteen (15). Any further information supplied on request. Applications accompanied by testimonials should set out name in full, age, qualifications, experience, marital status, war service (if any), and date applicant could commence duties and should be addressed to the Secretary, Hospitals Board, Cloncurry.

# Books on Science Medicine Technic



**GRAHAME BOOK COMPANY**  
PRUDENTIAL BUILDING  
39 MARTIN PLACE, SYDNEY, N.S.W.

## ATHERTON HOSPITALS BOARD: JUNIOR RESIDENT MEDICAL OFFICER.

Applications are invited for the position of Junior Resident Medical Officer at the Atherton Hospital, North Queensland. Salary classification: minimum £612, maximum £712, with sustenance allowance of £48. The minimum salary will be paid to applicants with one year's hospital service, with the maximum for applicants with two years' hospital service. A modern unfurnished brick residence, together with fuel and light, is provided. (The residence available is well furnished and a reasonable charge will be made for use of this furniture.) Duties are to assist the Medical Superintendent and to relieve him at any time he may be absent. Daily average 70. Out-patients 1,300 monthly. Fare refunded after twelve months. Applicants to enclose copy of references and to advise when would be able to take up duties. It is suggested that air mail post be used. Applications close on 5th January, 1949.—W. H. SHERRIN, Secretary.

## MEDICAL PRACTICES

Reliable Locum Tenens provided. Practices and Partnerships Transferred.

**MARTIN & CO SURGICAL PTY. LTD.**  
104 Hunter Street, Sydney.  
Phone: B 1539.

**JUNIOR PARTNER** wanted in Adelaide suburban practice, consisting of mainly private patients. Replies to No. 99, c.o. this office.

**ADVERTISEMENTS.**—Copy for advertisements in this section of the journal should be in the hands of the Manager ten days prior to date of publication. The rate is 10s. per single column inch, with a minimum charge of 6s.





for the epileptic...

# calm without the storm

Tridione, Abbott's new synthetic drug, has been shown by clinical tests to be effective in the treatment of petit mal seizures in which other drugs have proved ineffective. • In one series of tests<sup>1</sup> Tridione was given to a group of 50 patients subject to petit mal, myoclonic or akinetic seizures not helped by previous medication. In a period of days to weeks, these seizures ceased in 28 per cent. of the cases, were reduced to less than one-fourth of the usual number in 52 per cent., and were little affected in 20 per cent. In several patients the seizures once stopped *did not return* when medication was discontinued. Tridione also has had a beneficial effect in the control of psychomotor seizures in a certain proportion of cases.<sup>2</sup>

• Tridione is supplied in 0.3-Gm. capsules in bottles of 100.

Literature on Tridione will be mailed on request.

ABBOTT LABORATORIES (AUSTRALIA) PTY. LTD.,  
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## TRIDIONE

TRADE MARK

(3,5,5-trimethylxolidine-2,4-dione, Abbott)

- (1) Lemons, W. G. (1945), *Petit Mal Epilepsies: Their treatment With Tridione*, J. Amer. Med. Assn., 129:1009, December 15.
- (2) Dejong, R. N. (1946), *Effect of Tridione in the Control of Psychomotor Attacks*, J. Amer. Med. Assn., 130:585, March 2.

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